DBS EPILEPSY FACT SHEET

What is it?

The Medtronic Deep Brain Stimulation (DBS) System for Epilepsy is indicated as bilateral stimulation of the anterior nucleus of the thalamus (ANT) as an adjunctive therapy for reducing the frequency of seizures in individuals 18 years of age or older diagnosed with epilepsy characterized by partial-onset seizures (seizures originating from one cerebral hemisphere), with or without secondary generalization (spreading to the other hemisphere), that are refractory to three or more antiepileptic medications. The DBS system has demonstrated safety and effectiveness in patients who averaged six or more seizures per month over the three most recent months prior to system implant (with no more than 30 days between seizures). The Medtronic DBS System for Epilepsy has not been evaluated in patients with less frequent seizures. The FDA approved Medtronic's DBS System for Epilepsy on April 27, 2018. This therapy is similar to DBS for Parkinson's disease (available in the US since 2002) and DBS for essential tremor (available in the US since 1997); for example, implantable components for epilepsy are also indicated for Parkinson's disease and essential tremor. Since 1987, more than 175,000 patients worldwide have received Medtronic DBS Therapy.*

What are the treatment options for Epilepsy?

Guidelines recommend that adults with drug-resistant epilepsy be evaluated for their suitability for resective surgery (the removal of brain tissue using either an open procedure or laser-guided strategy). However, resective surgery is not an option for all patients. For drug-resistant epilepsy patients who are ineligible for, or refuse resective surgery, neurostimulation alternatives include DBS, Vagus Nerve Stimulation (VNS) and Responsive Neurostimulation (RNS).

What results can be expected from DBS therapy?[1]

- In Medtronic's randomized controlled clinical trial called "SANTÉ" (Stimulation of the Anterior Nucleus of the Thalamus in Epilepsy), the long-term safety and effectiveness for DBS Therapy for Epilepsy was established through 2–7 years.[2,3,4,5]
- At the end of the 3-month blinded phase of the study (final month), the median total seizure frequency reduction from baseline was 40.4% versus 14.5% for the placebo group. In addition, DBS significantly reduced patients' most severe seizures, complex partial seizures, and the incidence of epilepsy-related injury.[1,2]
- At year 7, patients experienced a median 75% reduction in seizure frequency from baseline, as assessed with open-label ongoing therapy. Seventy-four percent of patients were considered responders to DBS therapy and had experienced at least a 50% reduction in their seizures. Eighteen percent of patients were seizure-free for at least 6 consecutive months at any time between implant and year 7. Further, there were significant improvements in seizure severity and quality of life. Long-term, there was an improvement in seizure frequency from baseline in patient subgroups whom had tried VNS or had a prior resective surgery.[3]
- No significant cognitive declines or worsening of depression scores were observed through the blinded phase or in open-label at 7-years. Higher scores were observed at 7 years on measures of executive functions and attention.[5]
- Assessment of long-term safety, based on a minimum of 7 years of follow-up for all subjects active in the study, indicated the rate of intracranial hemorrhages (ICH) Serious Adverse Events (SAEs) was 0.9%, and resolved without sequelae or surgical intervention. Device-related intracranial hemorrhages were asymptomatic. The most frequent device-related SAEs were implant site infection (10.9%) and lead(s) not within target (8.2%), with all others reported in 1.8% of subjects or fewer. The majority of the device-related SAEs occurred during the Operative Phase. The SUDEP rate (2.5 per 1000 person-years) was not elevated compared to the rate reported in a similar patient population of epilepsy surgical candidates.[6]
- Overall, the clinical profile for DBS Therapy for Epilepsy demonstrates long-term improvements in epilepsy-related clinical symptoms, with 84% of patients (54/64) indicating they were satisfied or greatly satisfied with the results after 7 years.

Why is DBS therapy important to the treatment continuum?

DBS Therapy for Epilepsy is important to the treatment continuum because:

- Epilepsy may have a significant impact on a patient's quality of life.
- The therapy has been studied in a randomized controlled trial providing Class 1 evidence.
- Medtronic DBS systems are MR Conditional and are safe for MRI scans under certain conditions.**
- Medtronic DBS therapy does not require the seizure foci to be identified for patients with focal (partial-onset) seizures.
- Only 10-20% of the people with refractory epilepsy are good candidates for resective surgery; therefore, alternative treatment options such as DBS are needed.[7]

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Brief Statement: Medtronic DBS Therapy for Epilepsy

Medtronic DBS Therapy for Epilepsy: Product labeling must be reviewed prior to use for detailed disclosure of risks.

INDICATIONS: Bilateral stimulation of the anterior nucleus of the thalamus (ANT) using the Medtronic DBS System for Epilepsy is indicated as an adjunctive therapy for reducing the frequency of seizures in individuals 18 years of age or older diagnosed with epilepsy characterized by partial-onset seizures, with or without secondary generalization, that are refractory to three or more antiepileptic medications.

The Medtronic DBS System for Epilepsy has demonstrated safety and effectiveness for patients who average six or more seizures per month over the three most recent months prior to implant of the DBS system (with no more than 30 days between seizures). The Medtronic DBS System for Epilepsy has not been evaluated in patients with less frequent seizures.

CONTRAINDICATIONS: Medtronic DBS Therapy is contraindicated (not allowed) for patients who are unable to properly operate the neurostimulator. The following procedures are contraindicated for patients with DBS systems: diathermy (e.g., shortwave diathermy, microwave diathermy or therapeutic ultrasound diathermy), which can cause neurostimulation system or tissue damage and can result in severe injury or death; Transcranial Magnetic Stimulation (TMS); and certain MRI procedures using a full body transmit radio-frequency (RF) coil, a receive-only head coil, or a head transmit coil that extends over the chest area if the patient has an implanted Soletra™ Model 7426 Neurostimulator, Kinetra™ Model 7428 Neurostimulator, Activa™ SC Model 37602 Neurostimulator, or Model 64001 or 64002 pocket adaptor.

WARNINGS: There is a potential risk of brain tissue damage using stimulation parameter settings of high amplitudes and wide pulse widths. Extreme care should be used with lead implantation in patients with a heightened risk of intracranial hemorrhage. Sources of electromagnetic interference (EMI) may cause device damage or patient injury. Theft detectors and security screening devices may cause stimulation to switch ON or OFF and may cause some patients to experience a momentary increase in perceived stimulation. The DBS System may be affected by or adversely affect medical equipment such as cardiac pacemakers or therapies, cardioverter/defibrillators, external defibrillators, ultrasonic equipment, electrocautery, or radiation therapy. MRI conditions that may cause excessive heating at the lead electrodes which can result in serious and permanent injury including coma, paralysis, or death, or that may cause device damage, include: neurostimulator implant location other than pectoral and abdominal regions; unapproved MRI parameters; partial system explants ("abandoned systems"); misidentification of neurostimulator model numbers; and broken conductor wires (in the lead, extension or pocket adaptor). The safety of electroconvulsive therapy (ECT) in patients receiving DBS Therapy has not been established. Cessation, reduction, or initiation of stimulation may potentially lead to an increase in seizure frequency, severity, and new types of seizures. Symptoms may return with an intensity greater than was experienced prior to system implant, including the potential for status epilepticus. Depression, suicidal ideations and suicide have been reported in patients receiving Medtronic DBS Therapy for Epilepsy, although no direct cause-and-effect relationship has been established. Preoperatively, assess patients for depression and carefully balance this risk with the potential clinical benefit. Postoperatively, monitor patients closely for new or changing symptoms of depression and manage these symptoms appropriately. Patients should be monitored for memory impairment. Memory impairment has been reported in patients receiving Medtronic DBS Therapy for Epilepsy, although no direct cause-and-effect relationship has been established. The consequences of failing to monitor patients are unknown. When stimulation is adjusted, monitor patients for new or increased seizures, tingling sensation, change in mood, or confusion. Patients should avoid activities that may put undue stress on the implanted components of the neurostimulation system. Activities that include sudden, excessive or repetitive bending, twisting, or stretching can cause component fracture or dislodgement that may result in loss of stimulation, intermittent stimulation, stimulation at the fracture site, and additional surgery to replace or reposition the component. Patients should avoid manipulating the implanted system components or burr hole site as this can result in component damage, lead dislodgement, skin erosion, or stimulation at the implant site. Patients should not dive below 10 meters (33 feet) of water or enter hyperbaric chambers above 2.0 atmospheres absolute (ATA) as this could damage the neurostimulation system, before diving or using a hyperbaric chamber, patients should discuss the effects of high pressure with their clinician.

PRECAUTIONS: Loss of coordination in activities such as swimming may occur.

ADVERSE EVENTS: Adverse events related to the therapy, device, or procedure can include intracranial hemorrhage, cerebral infarction, CSF leak, pneumocephalus, seizures, surgical site complications (including pain, infection, dehiscence, erosion, seroma, and hematoma), meningitis, encephalitis, brain abscess, cerebral edema, aseptic cyst formation, device complications (including lead fracture and device migration) that may require revision or explant, extension fibrosis (tightening or bowstringing), new or exacerbation of neurological symptoms (including vision disorders, speech and swallowing disorders, motor coordination and balance disorders, sensory disturbances, cognitive impairment, and sleep disorders), psychiatric and behavioral disorders (including psychosis and abnormal thinking), cough, shocking or jolting sensation, ineffective therapy and weight gain or loss.

The safety and effectiveness of this therapy has not been established for patients without partial-onset seizures, patients who are pregnant or nursing, patients under the age of 18 years, patients with coagulopathies, and patients older than 65 years.

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**Based on sales information dated January 2020 and includes the following indications; Parkinson's disease, essential tremor, obsessive-compulsive disorder, dystonia, and epilepsy.*

***Medtronic DBS systems are MR Conditional and safe in the MR environment as long as certain conditions are met. If the conditions are not met, a significant risk is tissue lesions from component heating, especially at the lead electrodes, resulting in serious and permanent injury including coma, paralysis, or death. Refer to the MRI Guidelines for Medtronic Deep Brain Stimulation Systems for a complete list of conditions: http://professional.medtronic.com/mri.*

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PARKINSON'S DISEASE FACT SHEET

What is it?

The Medtronic Deep Brain Stimulation (DBS) System for Parkinson's disease (PD) is bilateral stimulation of the internal globus pallidus (GPi) or the subthalamic nucleus (STN) as an adjunctive therapy in reducing some of the symptoms in individuals with levodopa-responsive Parkinson's disease of at least 4 years' duration that are not adequately controlled with medication, including motor complications of recent onset (from 4 months to 3 years) or motor complications of longer-standing duration. Medtronic's DBS System obtained first CE Mark for advanced PD in 1998 and FDA approval in 2002. Since 1987, more than 175,000 patients worldwide have received Medtronic DBS Therapy.*

What are the treatment options for Parkinson's disease?

PD is a disease of the central nervous system. It is progressive, which means that symptoms get worse over time. Medications and surgical treatments may control movement symptoms of PD. Physical Therapy can also help. Treatment typically starts with medication. Medications may help reduce movement symptoms by increasing dopamine in the brain or mimicking its effects. Surgical options include DBS, levodopa-carbidopa intestinal pump, pallidotomy and thalamotomy.

What results can be expected from DBS therapy?[1]

Below is a summary of the first Level I randomized controlled trial of Medtronic DBS Therapy for Parkinson's disease that examines the impact of the therapy in patients with recent onset motor complications. The study is also the first to compare Medtronic DBS Therapy to best medical therapy (BMT) out to 24 months.[2]

MOTOR FUNCTION:

DBS (STN) patients with recent onset of motor complications achieved a 20% statistically significant improvement in time with good mobility and no troublesome dyskinesia (2.1 hours from baseline) compared to 2% (0.2 hours) with BMT alone at 24-month follow-up. "On" time without troublesome dyskinesia at baseline was 10.3 hours.[2]

In an off-medication condition, DBS (STN) therapy showed an improvement in Unified Parkinson's Disease Rating Scale (UPDRS) III of 53% from baseline to 24 months compared to 4% in patients with BMT alone in the study of patients with recent onset of motor complications.[2]

QUALITY OF LIFE:

Medtronic DBS along with Parkinson's medication improved quality of life (based on PDQ-39) at 24-months follow-up.[2] DBS (STN) patients showed a statistically significantly improvement of 26% versus a 1% decline in subjects receiving BMT alone.[2]

SAFETY:

- Overall serious adverse events (SAE) affected 55.6% of the DBS patients as compared to 44.1% of BMT alone patients in this clinical study of patients with recent-onset of motor complications at 24 months.[2]
- 99% of the serious adverse events were resolved at six months with or without sequelae.[2]

Medtronic

Below is a summary of a long-term randomized, controlled trial of Medtronic DBS Therapy for Parkinson's disease that examines the impact of the therapy in patients with longer-standing onset of motor complications. The study compared Medtronic DBS Therapy to BMT out to 6 months and 24 months with pooled STN and GPi target sites.[1]

MOTOR FUNCTION:
DBS patients gained up to 5.2 hours each day compared to 0 hours with BMT in the study of those with longer-standing motor complications at 6 months follow-up. DBS Therapy has a sustained improvement to 24 months with a 5.0 hour gain for STN and a 5.2 hour gain for GPi. "On" time without troublesome dyskinesias at baseline was only 6.4 hours.

In an off-medication condition, DBS therapy shows improvement (of at least 5 points in the UPDRS III). DBS improves 89% from baseline to 6 months compared to 37% in the patients with BMT alone in the study of patients with longer-standing motor complications. 83% of STN patients and 74% of GPi patients improve from baseline to 24 months.

QUALITY OF LIFE:
DBS improved PD related QOL by 20.6% vs. BMT at 6 months, and 12.6% STN and 12.5% GPI at 24 months as compared to baseline.

SAFETY:
- Overall serious adverse events (SAE) affected 56.5% of the STN patients and 51.0% of GPi patients in the Level 1 evidence clinical study of patients with longer-standing complications at 24 months.
- 99% of the serious adverse events are resolved at six months with or without sequelae.

What research has been done on Brain State?

Brain state sensing research began in 2013 using the Medtronic Activa™ PC+S system. The Activa™ PC+S system is an investigational system used for research related to brain state sensing; it is not approved by the FDA for commercial use. The following statements summarize evidence based on sensing local field potentials (LFPs) in research studies:***

- In patients with PD demonstrated to have measurable LFP signals in the beta band, those signals may be present and measured not only immediately following implant, but also for years post-implant.[3–7]
- Some publications suggest that LFP power measurements at select frequencies taken in-office in certain subgroups of PD patients may correlate to patient's symptomatic state, patient's medication state (on or off PD meds), and level of DBS stimulation.[3, 8–13]
- Elevated LFP power in beta band within STN may correlate with some clinical symptoms of patients with PD having predominantly akinetic-rigid symptoms as measured in office.[3,12–15]

Why is DBS therapy an important addition to the treatment continuum?

DBS Therapy for Parkinson's disease is an important addition to the treatment continuum because:

- Parkinson's disease may have a significant impact on a patient's quality of life.
- The therapy has been studied in 5 large randomized control trials.[2,16-20]
- Unlike other DBS manufacturers, Medtronic DBS systems are full-body** MR Conditional at 1.5T and 3T. Activa systems (1.5T) Percept System (1.5 and 3T).
- BrainSense™ Technology may be used to gather objective, personalized information on patients' disease status, inside and outside of the clinic.***
- Medtronic Percept™ PC Neurostimulator with BrainSense™ Technology is the only DBS system to chronically capture and record signals from the brain.***

** Based on sales information dated January 2020 and includes the following indications; Parkinson's disease, essential tremor, obsessive-compulsive disorder, dystonia, and epilepsy.*

*** Medtronic DBS systems are MR Conditional and safe in the MR environment as long as certain conditions are met. If the conditions are not met, a significant risk is tissue lesions from component heating, especially at the lead electrodes, resulting in serious and permanent injury including coma, paralysis, or death. Refer to the MRI Guidelines for Medtronic Deep Brain Stimulation Systems for a complete list of conditions http://professional.medtronic.com/mri*

**** Signals may not be present or measurable in all patients. Clinical benefits of brain sensing have not been established.*

Brief Statement: Medtronic DBS Therapy for Parkinson's Disease, Tremor, Dystonia, Obsessive-Compulsive Disorder, and Epilepsy

Medtronic DBS Therapy for Parkinson's Disease, Tremor, Dystonia, Obsessive-Compulsive Disorder, and Epilepsy: Product labeling must be reviewed prior to use for detailed disclosure of risks.

INDICATIONS:
Medtronic DBS Therapy for Parkinson's Disease: Bilateral stimulation of the internal globus pallidus (GPi) or the subthalamic nucleus (STN) using Medtronic DBS Therapy for Parkinson's Disease is indicated for adjunctive therapy in reducing some of the symptoms in individuals with levodopa-responsive Parkinson's disease of at least 4 years' duration that are not adequately controlled with medication, including motor complications of recent onset (from 4 months to 3 years) or motor complications of longer-standing duration.

Medtronic DBS Therapy for Tremor: Unilateral thalamic stimulation of the ventral intermediate nucleus (VIM) using Medtronic DBS Therapy for Tremor is indicated for the suppression of tremor in the upper extremity. The system is intended for use in patients who are diagnosed with essential tremor or parkinsonian tremor not adequately controlled by medications and where the tremor constitutes a significant functional disability.

Medtronic DBS Therapy for Dystonia*: Unilateral or bilateral stimulation of the internal globus pallidus (GPi) or the subthalamic nucleus (STN) using Medtronic DBS Therapy for Dystonia is indicated as an aid in the management of chronic, intractable (drug refractory) primary dystonia, including generalized and/or segmental dystonia, hemidystonia, and cervical dystonia (torticollis), in patients seven years of age or above.

Medtronic DBS Therapy for Obsessive-Compulsive Disorder*: The Medtronic Reclaim™ DBS Therapy is indicated for bilateral stimulation of the anterior limb of the internal capsule, AIC, as an adjunct to medications and as an alternative to anterior capsulotomy for treatment of chronic, severe, treatment-resistant obsessive-compulsive disorder (OCD) in adult patients who have failed at least three selective serotonin reuptake inhibitors (SSRIs).

Medtronic DBS Therapy for Epilepsy: Bilateral stimulation of the anterior nucleus of the thalamus (ANT) using the Medtronic DBS System for Epilepsy is indicated as an adjunctive therapy for reducing the frequency of seizures in individuals 18 years of age or older diagnosed with epilepsy characterized by partial-onset seizures, with or without secondary generalization, that are refractory to three or more antiepileptic medications.

The Medtronic DBS System for Epilepsy has demonstrated safety and effectiveness for patients who average six or more seizures per month over the three most recent months prior to implant of the DBS system (with no more than 30 days between seizures). The Medtronic DBS System for Epilepsy has not been evaluated in patients with less frequent seizures.

CONTRAINDICATIONS: Medtronic DBS Therapy is contraindicated (not allowed) for patients who are unable to properly operate the neurostimulator and, for Parkinson's disease and Essential Tremor, patients for whom test stimulation is unsuccessful. The following procedures are contraindicated for patients with DBS systems: diathermy (e.g., shortwave diathermy, microwave diathermy or therapeutic ultrasound diathermy), which can cause neurostimulation system or tissue damage and can result in severe injury or death; Transcranial Magnetic Stimulation (TMS); and certain MRI procedures using a full body transmit radio-frequency (RF) coil, a receive-only head coil, or a head transmit coil that extends over the chest area if they have an implanted Soletra™ Model 7426 Neurostimulator, Kinetra™ Model 7428 Neurostimulator, Activa™ SC Model 37602 Neurostimulator, or Model 64001 or 64002 pocket adaptor.

WARNINGS: There is a potential risk of brain tissue damage using stimulation parameter settings of high amplitudes and wide pulse widths and, for Parkinson's disease and Essential Tremor, a potential risk to drive tremor (cause tremor to occur at the same frequency as the programmed frequency) using low frequency settings. Extreme care should be used with lead implantation in patients with an increased risk of intracranial hemorrhage. Sources of electromagnetic interference (EMI) may cause device damage or patient injury. Theft detectors and security screening devices may cause stimulation to switch ON or OFF and may cause some patients to experience a momentary increase in perceived stimulation. The DBS System may be affected by or adversely affect medical equipment such as cardiac pacemakers or therapies, cardioverter/defibrillators, external defibrillators, ultrasonic equipment, electrocautery, or radiation therapy. MRI conditions that may cause excessive heating at the lead electrodes which can result in serious and permanent injury including coma, paralysis, or death, or that may cause device damage, include: neurostimulator implant location other than pectoral and abdominal regions; unapproved MRI parameters; partial system explants ("abandoned systems"); misidentification of neurostimulator model numbers; and broken conductor wires (in the lead, extension or pocket adaptor). The safety of electroconvulsive therapy (ECT) in patients receiving DBS Therapy has not been established. Abrupt cessation of stimulation should be avoided as it may cause a return of disease symptoms, in some cases with intensity greater than was experienced prior to system implant ("rebound" effect). Onset of status dystonicus, which may be life-threatening, may occur in dystonia patients during ongoing or loss of DBS therapy.

For Epilepsy, cessation, reduction, or initiation of stimulation may potentially lead to an increase in seizure frequency, severity, and new types of seizures. For Epilepsy, symptoms may return with an intensity greater than was experienced prior to system implant, including the potential for status epilepticus. For Parkinson's disease or essential tremor, new onset or worsening depression, suicidal ideation, suicide attempts, and suicide have been reported. For Dystonia or Epilepsy, depression, suicidal ideations and suicide have been reported, although no direct cause-and-effect relationship has been established. For Epilepsy, preoperatively, assess patients for depression and carefully balance this risk with the potential clinical benefit. Postoperatively, monitor patients closely for new or changing symptoms of depression and manage these systems appropriately. Patients should be monitored for memory impairment. Memory impairment has been reported in patients receiving Medtronic DBS Therapy for Epilepsy, although no direct-cause-and effect relationship has been established. The consequences of failing to monitor patients are unknown. When stimulation is adjusted, monitor patients for new or increased seizures, tingling sensation, change in mood, or confusion. For Obsessive-Compulsive Disorder, patients should be monitored for at least 30 minutes after a programming session for side effects, including: autonomic effects (e.g., facial flushing, facial muscle contractions, or increased heart rate), hypomania, increased disease symptoms, and sensations such as tingling, smell, or taste. For Obsessive-Compulsive Disorder, during treatment, patients should be monitored closely for increased depression, anxiety, suicidality, and worsening of obsessive-compulsive symptoms.

Patients should avoid activities that may put undue stress on the implanted components of the neurostimulation system. Activities that include sudden, excessive or repetitive bending, twisting, or stretching can cause component fracture or dislodgement that may result in loss of stimulation, intermittent stimulation, stimulation at the fracture site, and additional surgery to replace or reposition the component. Patients should avoid manipulating the implanted system components or burr hole site as this can result in component damage, lead dislodgement, skin erosion, or stimulation at the implant site. Patients should not dive below 10 meters (33 feet) of water or enter hyperbaric chambers above 2.0 atmospheres absolute (ATA) as this could damage the neurostimulation system, before diving or using a hyperbaric chamber, patients should discuss the effects of high pressure with their clinician.

Patients using a rechargeable neurostimulator for Parkinson's disease or essential tremor must not place the recharger over a medical device with which it is not compatible (eg, other neurostimulators, pacemaker, defibrillator, insulin pump). The recharger could accidentally change the operation of the medical device, which could result in a medical emergency. Patients should not use the recharger on an unhealed wound as the recharger system is not sterile and contact with the wound may cause an infection.

Warning For Obsessive-Compulsive Disorder:

Electroconvulsive Therapy (ECT) – The safety of ECT in patients who have an implanted deep brain stimulation (DBS) system has not been established. Induced electrical currents may interfere with the intended stimulation or damage the neurostimulation system components resulting in loss of therapeutic effect, clinically significant undesirable stimulation effects, additional surgery for system explantation and replacement, or neurological injury.

PRECAUTIONS: Loss of coordination in activities such as swimming may occur. For Obsessive-Compulsive Disorder, the safety of somatic psychiatric therapies using equipment that generates electromagnetic interference (e.g., vagus nerve stimulation) has not been established. Patients using a rechargeable neurostimulator for Parkinson's disease or essential tremor should check for skin irritation or redness near the neurostimulator during or after recharging, and contact their physician if symptoms persist.

ADVERSE EVENTS: Adverse events related to the therapy, device, or procedure can include intracranial hemorrhage, cerebral infarction, CSF leak, pneumocephalus, seizures, surgical site complications (including pain, infection, dehiscence, erosion, seroma, and hematoma), meningitis, encephalitis, brain abscess, cerebral edema, aseptic cyst formation, device complications (including lead fracture and device migration) that may require revision or explant, extension fibrosis (tightening or bowstringing), new or exacerbation of neurological symptoms (including vision disorders, speech and swallowing disorders, motor coordination and balance disorders, sensory disturbances, cognitive impairment, and sleep disorders), psychiatric and behavioral disorders (including psychosis and abnormal thinking), cough, shocking or jolting sensation, ineffective therapy, and weight gain or loss.

For Parkinson's disease or essential tremor, safety and effectiveness has not been established for patients with neurological disease other than idiopathic Parkinson's disease or Essential Tremor, previous surgical ablation procedures, dementia, coagulopathies, or moderate to severe depression, patients who are pregnant, or patients under 18 years. For Essential Tremor, safety and effectiveness has not been established for bilateral stimulation or for patients over 80 years of age. For Dystonia, safety of this device for use in the treatment of dystonia with or without other accompanying conditions (e.g., previous surgical ablation procedure, dementia, coagulopathies, or moderate to severe depression, or for patient who are pregnant) has not been established. Age of implant is suggested to be that at which brain growth is approximately 90% complete or above. For Epilepsy, the safety and effectiveness of this therapy has not been established for patients without partial-onset seizures, patients who are pregnant or nursing, patients under the age of 18 years, patients with coagulopathies, and patients older than 65 years. For Obsessive-Compulsive Disorder, the safety and probable benefit of this therapy has not been established for patients with: Tourette's syndrome, OCD with a subclassification of hoarding, previous surgical ablation (e.g., capsulotomy), dementia, coagulopathies or who are on anticoagulant therapy, neurological disorders, and other serious medical illness including cardiovascular disease, renal or hepatic failure, and diabetes mellitus. In addition, the safety and probable benefit has not been established for these patients: those whose diagnosis of OCD is documented to be less than 5 years duration or whose YBOCS score is less than 30, who have not completed a minimum of 3 adequate trials of first and/or second line medications with augmentation, who have not attempted to complete an adequate trial of cognitive behavior therapy (CBT), who are pregnant, who are under the age of 18 years, and who do not have comorbid depression and anxiety. Physicians should carefully consider the potential risks of implanting the Reclaim DBS System in patients with comorbid psychiatric disorders (e.g., bipolar, body dysmorphic, psychotic) as the Reclaim DBS System may aggravate the symptoms.

***Humanitarian Device:** The effectiveness of these devices for the treatment of dystonia and obsessive-compulsive disorder has not been demonstrated.

USA Rx only Rev 02/20

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ESSENTIAL TREMOR FACT SHEET

What is it?

The Medtronic Deep Brain Stimulation (DBS) System for essential tremor (ET) is unilateral thalamic stimulation of the ventral intermediate nucleus (VIM) and is indicated for the suppression of tremor in the upper extremity. The system is intended for use in patients who are diagnosed with essential tremor or parkinsonian tremor not adequately controlled by medications and where the tremor constitutes a significant functional disability. Medtronic's DBS System obtained CE Mark in 1993 for essential tremor, CE Mark for Parkinsonian tremor in 1995, and FDA approval for essential tremor and parkinsonian tremor in 1997. Since 1987, more than 175,000 patients worldwide have received Medtronic DBS Therapy.*

What are the treatment options for essential tremor?

Essential tremor is a disorder of the nervous system that causes a rhythmic shaking of a part of the body, most commonly hands. It can also affect the head, voice, arms, or legs. Often the symptoms begin gradually. People who have mild symptoms may cope for years without treatment, though they can become frustrated and limited by their tremor. Unfortunately, for many, the symptoms get worse and can be severe. A medication is often tried first. Many people find that medications do not work to control their tremor, and can have intolerable side effects like sleepiness, dizziness, or thinking problems.[1] Surgical options for ET include DBS, focused ultrasound thalamotomy, and radiosurgical (Gamma Knife®) thalamotomy.

What results can be expected from DBS therapy?[2]

Based on Medtronic's US Tremor Trial, the suppression of tremor due to essential tremor or Parkinson's disease was evaluated at 1, 3, 6, 9, and 12 months post-implant. Below are key findings:

- Activities of daily living (ADL) showed statistically significant improvement in 7 scales for essential tremor patients.
- Patients' assessment (subjective evaluation) of their disability was improved in both groups when compared to a pre-implant assessment.
- A maximum of 29% of Parkinson's disease patients, and 28% of essential tremor patients experienced rebound (return of symptoms) lasting for a mean duration of 17 minutes and 22 minutes, respectively. Rebound generally stabilizes (returns to normal) within approximately 30 minutes.

Why is DBS therapy an important addition to the treatment continuum?

DBS Therapy for essential tremor is an important addition to the treatment continuum because:

- ET may have a significant impact on a patient's activities of daily living.[3]
- ET is often confused with Parkinson's disease although it's eight times more common, affecting an estimated 10 million Americans and millions more worldwide.[3]
- Essential tremor (ET) is one of the most common movement disorders, yet only about 60 percent of patients receive satisfactory benefit from the currently available medications.[3]
- Unlike other DBS manufacturers, Medtronic DBS systems are full-body MR Conditional** at 1.5T and 3T. Activa™ systems (1.5T) Percept™ Systems (1.5 and 3T).

** Based on sales information dated January 2020 and includes the following indications; Parkinson's disease, essential tremor, obsessive-compulsive disorder, dystonia, and epilepsy.*

*** Medtronic DBS systems are MR Conditional and safe in the MR environment as long as certain conditions are met. If the conditions are not met, a significant risk is tissue lesions from component heating, especially at the lead electrodes, resulting in serious and permanent injury including coma, paralysis, or death. Refer to the MRI Guidelines for Medtronic Deep Brain Stimulation Systems for a complete list of conditions: http:// professional.medtronic.com/mri.*

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Brief Statement: Medtronic DBS Therapy for Parkinson's Disease, Tremor, Dystonia, Obsessive-Compulsive Disorder, and Epilepsy

Medtronic DBS Therapy for Parkinson's Disease, Tremor, Dystonia, Obsessive-Compulsive Disorder, and Epilepsy: Product labeling must be reviewed prior to use for detailed disclosure of risks.

INDICATIONS:
Medtronic DBS Therapy for Parkinson's Disease: Bilateral stimulation of the internal globus pallidus (GPi) or the subthalamic nucleus (STN) using Medtronic DBS Therapy for Parkinson's Disease is indicated for adjunctive therapy in reducing some of the symptoms in individuals with levodopa-responsive Parkinson's disease of at least 4 years' duration that are not adequately controlled with medication, including motor complications of recent onset (from 4 months to 3 years) or motor complications of longer-standing duration.

Medtronic DBS Therapy for Tremor: Unilateral thalamic stimulation of the ventral intermediate nucleus (VIM) using Medtronic DBS Therapy for Tremor is indicated for the suppression of tremor in the upper extremity. The system is intended for use in patients who are diagnosed with essential tremor or parkinsonian tremor not adequately controlled by medications and where the tremor constitutes a significant functional disability.

Medtronic DBS Therapy for Dystonia*: Unilateral or bilateral stimulation of the internal globus pallidus (GPi) or the subthalamic nucleus (STN) using Medtronic DBS Therapy for Dystonia is indicated as an aid in the management of chronic, intractable (drug refractory) primary dystonia, including generalized and/or segmental dystonia, hemidystonia, and cervical dystonia (torticollis), in patients seven years of age or above.

Medtronic DBS Therapy for Obsessive-Compulsive Disorder*: The Medtronic Reclaim™ DBS Therapy is indicated for bilateral stimulation of the anterior limb of the internal capsule, AIC, as an adjunct to medications and as an alternative to anterior capsulotomy for treatment of chronic, severe, treatment-resistant obsessive-compulsive disorder (OCD) in adult patients who have failed at least three selective serotonin reuptake inhibitors (SSRIs).

Medtronic DBS Therapy for Epilepsy: Bilateral stimulation of the anterior nucleus of the thalamus (ANT) using the Medtronic DBS System for Epilepsy is indicated as an adjunctive therapy for reducing the frequency of seizures in individuals 18 years of age or older diagnosed with epilepsy characterized by partial-onset seizures, with or without secondary generalization, that are refractory to three or more antiepileptic medications.

The Medtronic DBS System for Epilepsy has demonstrated safety and effectiveness for patients who average six or more seizures per month over the three most recent months prior to implant of the DBS system (with no more than 30 days between seizures). The Medtronic DBS System for Epilepsy has not been evaluated in patients with less frequent seizures.

CONTRAINDICATIONS: Medtronic DBS Therapy is contraindicated (not allowed) for patients who are unable to properly operate the neurostimulator and, for Parkinson's disease and Essential Tremor, patients for whom test stimulation is unsuccessful. The following procedures are contraindicated for patients with DBS systems: diathermy (e.g., shortwave diathermy, microwave diathermy or therapeutic ultrasound diathermy), which can cause neurostimulation system or tissue damage and can result in severe injury or death; Transcranial Magnetic Stimulation (TMS); and certain MRI procedures using a full body transmit radio-frequency (RF) coil, a receive-only head coil, or a head transmit coil that extends over the chest area if they have an implanted Soletra™ Model 7426 Neurostimulator, Kinetra™ Model 7428 Neurostimulator, Activa™ SC Model 37602 Neurostimulator, or Model 64001 or 64002 pocket adaptor.

WARNINGS: There is a potential risk of brain tissue damage using stimulation parameter settings of high amplitudes and wide pulse widths and, for Parkinson's disease and Essential Tremor, a potential risk to drive tremor (cause tremor to occur at the same frequency as the programmed frequency) using low frequency settings. Extreme care should be used with lead implantation in patients with an increased risk of intracranial hemorrhage. Sources of electromagnetic interference (EMI) may cause device damage or patient injury. Theft detectors and security screening devices may cause stimulation to switch ON or OFF and may cause some patients to experience a momentary increase in perceived stimulation. The DBS System may be affected by or adversely affect medical equipment such as cardiac pacemakers or therapies, cardioverter/defibrillators, external defibrillators, ultrasonic equipment, electrocautery, or radiation therapy. MRI conditions that may cause excessive heating at the lead electrodes which can result in serious and permanent injury including coma, paralysis, or death, or that may cause device damage, include: neurostimulator implant location other than pectoral and abdominal regions; unapproved MRI parameters; partial system explants ("abandoned systems"); misidentification of neurostimulator model numbers; and broken conductor wires (in the lead, extension or pocket adaptor). The safety of electroconvulsive therapy (ECT) in patients receiving DBS Therapy has not been established. Abrupt cessation of stimulation should be avoided as it may cause a return of disease symptoms, in some cases with intensity greater than was experienced prior to system implant ("rebound" effect). Onset of status dystonicus, which may be life-threatening, may occur in dystonia patients during ongoing or loss of DBS therapy.

For Epilepsy, cessation, reduction, or initiation of stimulation may potentially lead to an increase in seizure frequency, severity, and new types of seizures. For Epilepsy, symptoms may return with an intensity greater than was experienced prior to system implant, including the potential for status epilepticus. For Parkinson's disease or essential tremor, new onset or worsening depression, suicidal ideation, suicide attempts, and suicide have been reported. For Dystonia or Epilepsy, depression, suicidal ideations and suicide have been reported, although no direct cause-and-effect relationship has been established. For Epilepsy, preoperatively, assess patients for depression and carefully balance this risk with the potential clinical benefit. Postoperatively, monitor patients closely for new or changing symptoms of depression and manage these systems appropriately. Patients should be monitored for memory impairment. Memory impairment has been reported in patients receiving Medtronic DBS Therapy for Epilepsy, although no direct-cause-and effect relationship has been established. The consequences of failing to monitor patients are unknown. When stimulation is adjusted, monitor patients for new or increased seizures, tingling sensation, change in mood, or confusion. For Obsessive-Compulsive Disorder, patients should be monitored for at least 30 minutes after a programming session for side effects, including: autonomic effects (e.g., facial flushing, facial muscle contractions, or increased heart rate), hypomania, increased disease symptoms, and sensations such as tingling, smell, or taste. For Obsessive-Compulsive Disorder, during treatment, patients should be monitored closely for increased depression, anxiety, suicidality, and worsening of obsessive-compulsive symptoms.

Patients should avoid activities that may put undue stress on the implanted components of the neurostimulation system. Activities that include sudden, excessive or repetitive bending, twisting, or stretching can cause component fracture or dislodgement that may result in loss of stimulation, intermittent stimulation, stimulation at the fracture site, and additional surgery to replace or reposition the component. Patients should avoid manipulating the implanted system components or burr hole site as this can result in component damage, lead dislodgement, skin erosion, or stimulation at the implant site. Patients should not dive below 10 meters (33 feet) of water or enter hyperbaric chambers above 2.0 atmospheres absolute (ATA) as this could damage the neurostimulation system, before diving or using a hyperbaric chamber, patients should discuss the effects of high pressure with their clinician.

Patients using a rechargeable neurostimulator for Parkinson's disease or essential tremor must not place the recharger over a medical device with which it is not compatible (eg, other neurostimulators, pacemaker, defibrillator, insulin pump). The recharger could accidentally change the operation of the medical device, which could result in a medical emergency. Patients should not use the recharger on an unhealed wound as the recharger system is not sterile and contact with the wound may cause an infection.

Warning For Obsessive-Compulsive Disorder:

Electroconvulsive Therapy (ECT) – The safety of ECT in patients who have an implanted deep brain stimulation (DBS) system has not been established. Induced electrical currents may interfere with the intended stimulation or damage the neurostimulation system components resulting in loss of therapeutic effect, clinically significant undesirable stimulation effects, additional surgery for system explantation and replacement, or neurological injury.

PRECAUTIONS: Loss of coordination in activities such as swimming may occur. For Obsessive-Compulsive Disorder, the safety of somatic psychiatric therapies using equipment that generates electromagnetic interference (e.g., vagus nerve stimulation) has not been established. Patients using a rechargeable neurostimulator for Parkinson's disease or essential tremor should check for skin irritation or redness near the neurostimulator during or after recharging, and contact their physician if symptoms persist.

ADVERSE EVENTS: Adverse events related to the therapy, device, or procedure can include intracranial hemorrhage, cerebral infarction, CSF leak, pneumocephalus, seizures, surgical site complications (including pain, infection, dehiscence, erosion, seroma, and hematoma), meningitis, encephalitis, brain abscess, cerebral edema, aseptic cyst formation, device complications (including lead fracture and device migration) that may require revision or explant, extension fibrosis (tightening or bowstringing), new or exacerbation of neurological symptoms (including vision disorders, speech and swallowing disorders, motor coordination and balance disorders, sensory disturbances, cognitive impairment, and sleep disorders), psychiatric and behavioral disorders (including psychosis and abnormal thinking), cough, shocking or jolting sensation, ineffective therapy, and weight gain or loss.

For Parkinson's disease or essential tremor, safety and effectiveness has not been established for patients with neurological disease other than idiopathic Parkinson's disease or Essential Tremor, previous surgical ablation procedures, dementia, coagulopathies, or moderate to severe depression, patients who are pregnant, or patients under 18 years. For Essential Tremor, safety and effectiveness has not been established for bilateral stimulation or for patients over 80 years of age. For Dystonia, safety of this device for use in the treatment of dystonia with or without other accompanying conditions (e.g., previous surgical ablation procedure, dementia, coagulopathies, or moderate to severe depression, or for patient who are pregnant) has not been established. Age of implant is suggested to be that at which brain growth is approximately 90% complete or above. For Epilepsy, the safety and effectiveness of this therapy has not been established for patients without partial-onset seizures, patients who are pregnant or nursing, patients under the age of 18 years, patients with coagulopathies, and patients older than 65 years. For Obsessive-Compulsive Disorder, the safety and probable benefit of this therapy has not been established for patients with: Tourette's syndrome, OCD with a subclassification of hoarding, previous surgical ablation (e.g., capsulotomy), dementia, coagulopathies or who are on anticoagulant therapy, neurological disorders, and other serious medical illness including cardiovascular disease, renal or hepatic failure, and diabetes mellitus. In addition, the safety and probable benefit has not been established for these patients: those whose diagnosis of OCD is documented to be less than 5 years duration or whose YBOCS score is less than 30, who have not completed a minimum of 3 adequate trials of first and/or second line medications with augmentation, who have not attempted to complete an adequate trial of cognitive behavior therapy (CBT), who are pregnant, who are under the age of 18 years, and who do not have comorbid depression and anxiety. Physicians should carefully consider the potential risks of implanting the Reclaim DBS System in patients with comorbid psychiatric disorders (e.g., bipolar, body dysmorphic, psychotic) as the Reclaim DBS System may aggravate the symptoms.

***Humanitarian Device:** The effectiveness of these devices for the treatment of dystonia and obsessive-compulsive disorder has not been demonstrated.

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DYSTONIA* FACT SHEET

What is it?

The Medtronic Deep Brain Stimulation (DBS) System for dystonia is unilateral or bilateral stimulation of the internal globus pallidus (GPi) or the subthalamic nucleus (STN) indicated as an aid in the management of chronic, intractable (drug refractory) primary dystonia, including generalized and/or segmental dystonia, hemidystonia, and cervical dystonia (torticollis), in patients seven years of age or above. Deep brain stimulation started in 1987 and in 2003, Medtronic DBS Therapy for Dystonia was approved by the FDA. More than 175,000 patients worldwide have received from Medtronic DBS Therapy.**

What are the treatment options for dystonia?

Dystonia is a neurological movement disorder characterized by involuntary muscle contractions. These contractions force certain parts of the body into repetitive, twisting movements or painful postures that may interfere with everyday functions like walking, sleeping, eating, and talking. Although dystonia has no cure, there are several treatments such as medication and injections, drug therapies, rhizotomy and pallidotomy, and DBS therapy.

Safety and Probable Benefit of DBS Therapy[1,2]

The safety and probable benefit of DBS Therapy for dystonia is approved by the FDA under a Humanitarian Device Exemption (HDE). The therapy delivers stimulation to targeted areas of the brain that may decrease some or all symptoms. Symptoms will return when the stimulation is turned off.

During DBS Therapy, a small, pacemaker-like device sends electrical signals to an area in the brain that controls movement. These signals block some of the brain messages that cause frustrating and disabling motor symptoms. The device is placed under the skin in the chest (or abdomen). Very thin wires connect the device to the brain to enable the signals to reach the source of symptoms. Most people don't feel the stimulation at all as it reduces their symptoms. Some people may feel a brief tingling when the stimulation is first turned on. Following the procedure, stimulation settings are adjusted by the physician to manage individual symptoms. The physician may provide the patient with a small hand-held programmer to adjust stimulation withing physician set limits, and turn the device on and off. Over time, settings can be adjusted by physicians as symptoms change. A few weeks after the procedure, people can go back to normal daily activities following their physician's instructions.

The stimulation targets used in DBS Therapy for dystonia as well as the implant procedure are the same as for DBS Therapy for Parkinson's disease and DBS Therapy for essential tremor. Therefore, risks associated with DBS Therapy for dystonia are similar to risks associated with DBS Therapy for Parkinson's disease or essential tremor. DBS Therapy is not for everyone. DBS Therapy requires brain surgery which can have serious and sometimes fatal complications. Other complications can occur and may require additional surgery. DBS Therapy may cause new or worsening neurological or psychiatric symptoms. In patients receiving DBS Therapy for dystonia, depression, suicidal ideations, and suicide have been reported, although no direct cause-and-effect relationship has been established. Onset of status dystonicus, which may be life-threatening, may occur in dystonia patients during ongoing or loss of DBS Therapy.

Why is DBS therapy important to the treatment continuum?

Dystonia is a challenging disease complex to treat because the various pathophysiologies leading to the disease conditions are not well understood. No cures and no treatments exist to reverse the course of the disorder. Medtronic DBS therapy for patients with dystonia is considered advantageous because:[3]

- treatment is reversible (device can be turned off or removed;
- stimulation parameters are adjustable for optimal therapy; and
- DBS therapy is non-destructive, an especially important feature in a developing brain because is does not foreclose the possibility for future therapeutic interventions.

Unlike other DBS manufacturers, Medtronic DBS systems are full-body MR Conditional** at 1.5T and 3T. Activa systems (1.5T) Percept Systems (1.5 and 3T).

The probable benefit to health from the use of Medtronic DBS therapy for dystonia outweighs the risk of injury or illness from its use.

* ***Humanitarian Device:*** *The effectiveness of the devices for the treatment of dystonia has not been demonstrated.*

** *Based on sales information dated January 2020 and includes the following indications; Parkinson's disease, essential tremor, obsessive-compulsive disorder, dystonia, and epilepsy.*

*** *Medtronic DBS systems are MR Conditional and safe in the MR environment as long as certain conditions are met. If the conditions are not met, a significant risk is tissue lesions from component heating, especially at the lead electrodes, resulting in serious and permanent injury including coma, paralysis, or death. Refer to the MRI Guidelines for Medtronic Deep Brain Stimulation Systems for a complete list of conditions: http:// professional.medtronic.com/mri.*

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Brief Statement: Medtronic DBS Therapy for Parkinson's Disease, Tremor, Dystonia, Obsessive-Compulsive Disorder, and Epilepsy

Medtronic DBS Therapy for Parkinson's Disease, Tremor, Dystonia, Obsessive-Compulsive Disorder, and Epilepsy: Product labeling must be reviewed prior to use for detailed disclosure of risks.

INDICATIONS:
Medtronic DBS Therapy for Parkinson's Disease: Bilateral stimulation of the internal globus pallidus (GPi) or the subthalamic nucleus (STN) using Medtronic DBS Therapy for Parkinson's Disease is indicated for adjunctive therapy in reducing some of the symptoms in individuals with levodopa-responsive Parkinson's disease of at least 4 years' duration that are not adequately controlled with medication, including motor complications of recent onset (from 4 months to 3 years) or motor complications of longer-standing duration.

Medtronic DBS Therapy for Tremor: Unilateral thalamic stimulation of the ventral intermediate nucleus (VIM) using Medtronic DBS Therapy for Tremor is indicated for the suppression of tremor in the upper extremity. The system is intended for use in patients who are diagnosed with essential tremor or parkinsonian tremor not adequately controlled by medications and where the tremor constitutes a significant functional disability.

Medtronic DBS Therapy for Dystonia*: Unilateral or bilateral stimulation of the internal globus pallidus (GPi) or the subthalamic nucleus (STN) using Medtronic DBS Therapy for Dystonia is indicated as an aid in the management of chronic, intractable (drug refractory) primary dystonia, including generalized and/or segmental dystonia, hemidystonia, and cervical dystonia (torticollis), in patients seven years of age or above.

Medtronic DBS Therapy for Obsessive-Compulsive Disorder*: The Medtronic Reclaim™ DBS Therapy is indicated for bilateral stimulation of the anterior limb of the internal capsule, AIC, as an adjunct to medications and as an alternative to anterior capsulotomy for treatment of chronic, severe, treatment-resistant obsessive-compulsive disorder (OCD) in adult patients who have failed at least three selective serotonin reuptake inhibitors (SSRIs).

Medtronic DBS Therapy for Epilepsy: Bilateral stimulation of the anterior nucleus of the thalamus (ANT) using the Medtronic DBS System for Epilepsy is indicated as an adjunctive therapy for reducing the frequency of seizures in individuals 18 years of age or older diagnosed with epilepsy characterized by partial-onset seizures, with or without secondary generalization, that are refractory to three or more antiepileptic medications.

The Medtronic DBS System for Epilepsy has demonstrated safety and effectiveness for patients who average six or more seizures per month over the three most recent months prior to implant of the DBS system (with no more than 30 days between seizures). The Medtronic DBS System for Epilepsy has not been evaluated in patients with less frequent seizures.

CONTRAINDICATIONS: Medtronic DBS Therapy is contraindicated (not allowed) for patients who are unable to properly operate the neurostimulator and, for Parkinson's disease and Essential Tremor, patients for whom test stimulation is unsuccessful. The following procedures are contraindicated for patients with DBS systems: diathermy (e.g., shortwave diathermy, microwave diathermy or therapeutic ultrasound diathermy), which can cause neurostimulation system or tissue damage and can result in severe injury or death; Transcranial Magnetic Stimulation (TMS); and certain MRI procedures using a full body transmit radio-frequency (RF) coil, a receive-only head coil, or a head transmit coil that extends over the chest area if they have an implanted Soletra™ Model 7426 Neurostimulator, Kinetra™ Model 7428 Neurostimulator, Activa™ SC Model 37602 Neurostimulator, or Model 64001 or 64002 pocket adaptor.

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For Epilepsy, cessation, reduction, or initiation of stimulation may potentially lead to an increase in seizure frequency, severity, and new types of seizures. For Epilepsy, symptoms may return with an intensity greater than was experienced prior to system implant, including the potential for status epilepticus. For Parkinson's disease or essential tremor, new onset or worsening depression, suicidal ideation, suicide attempts, and suicide have been reported. For Dystonia or Epilepsy, depression, suicidal ideations and suicide have been reported, although no direct cause-and-effect relationship has been established. For Epilepsy, preoperatively, assess patients for depression and carefully balance this risk with the potential clinical benefit. Postoperatively, monitor patients closely for new or changing symptoms of depression and manage these systems appropriately. Patients should be monitored for memory impairment. Memory impairment has been reported in patients receiving Medtronic DBS Therapy for Epilepsy, although no direct-cause-and effect relationship has been established. The consequences of failing to monitor patients are unknown. When stimulation is adjusted, monitor patients for new or increased seizures, tingling sensation, change in mood, or confusion. For Obsessive-Compulsive Disorder, patients should be monitored for at least 30 minutes after a programming session for side effects, including: autonomic effects (e.g., facial flushing, facial muscle contractions, or increased heart rate), hypomania, increased disease symptoms, and sensations such as tingling, smell, or taste. For Obsessive-Compulsive Disorder, during treatment, patients should be monitored closely for increased depression, anxiety, suicidality, and worsening of obsessive-compulsive symptoms.

Patients should avoid activities that may put undue stress on the implanted components of the neurostimulation system. Activities that include sudden, excessive or repetitive bending, twisting, or stretching can cause component fracture or dislodgement that may result in loss of stimulation, intermittent stimulation, stimulation at the fracture site, and additional surgery to replace or reposition the component. Patients should avoid manipulating the implanted system components or burr hole site as this can result in component damage, lead dislodgement, skin erosion, or stimulation at the implant site. Patients should not dive below 10 meters (33 feet) of water or enter hyperbaric chambers above 2.0 atmospheres absolute (ATA) as this could damage the neurostimulation system, before diving or using a hyperbaric chamber, patients should discuss the effects of high pressure with their clinician.

Patients using a rechargeable neurostimulator for Parkinson's disease or essential tremor must not place the recharger over a medical device with which it is not compatible (eg, other neurostimulators, pacemaker, defibrillator, insulin pump). The recharger could accidentally change the operation of the medical device, which could result in a medical emergency. Patients should not use the recharger on an unhealed wound as the recharger system is not sterile and contact with the wound may cause an infection.

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ADVERSE EVENTS: Adverse events related to the therapy, device, or procedure can include intracranial hemorrhage, cerebral infarction, CSF leak, pneumocephalus, seizures, surgical site complications (including pain, infection, dehiscence, erosion, seroma, and hematoma), meningitis, encephalitis, brain abscess, cerebral edema, aseptic cyst formation, device complications (including lead fracture and device migration) that may require revision or explant, extension fibrosis (tightening or bowstringing), new or exacerbation of neurological symptoms (including vision disorders, speech and swallowing disorders, motor coordination and balance disorders, sensory disturbances, cognitive impairment, and sleep disorders), psychiatric and behavioral disorders (including psychosis and abnormal thinking), cough, shocking or jolting sensation, ineffective therapy, and weight gain or loss.

For Parkinson's disease or essential tremor, safety and effectiveness has not been established for patients with neurological disease other than idiopathic Parkinson's disease or Essential Tremor, previous surgical ablation procedures, dementia, coagulopathies, or moderate to severe depression, patients who are pregnant, or patients under 18 years. For Essential Tremor, safety and effectiveness has not been established for bilateral stimulation or for patients over 80 years of age. For Dystonia, safety of this device for use in the treatment of dystonia with or without other accompanying conditions (e.g., previous surgical ablation procedure, dementia, coagulopathies, or moderate to severe depression, or for patient who are pregnant) has not been established. Age of implant is suggested to be that at which brain growth is approximately 90% complete or above. For Epilepsy, the safety and effectiveness of this therapy has not been established for patients without partial-onset seizures, patients who are pregnant or nursing, patients under the age of 18 years, patients with coagulopathies, and patients older than 65 years. For Obsessive-Compulsive Disorder, the safety and probable benefit of this therapy has not been established for patients with: Tourette's syndrome, OCD with a subclassification of hoarding, previous surgical ablation (e.g., capsulotomy), dementia, coagulopathies or who are on anticoagulant therapy, neurological disorders, and other serious medical illness including cardiovascular disease, renal or hepatic failure, and diabetes mellitus. In addition, the safety and probable benefit has not been established for these patients: those whose diagnosis of OCD is documented to be less than 5 years duration or whose YBOCS score is less than 30, who have not completed a minimum of 3 adequate trials of first and/or second line medications with augmentation, who have not attempted to complete an adequate trial of cognitive behavior therapy (CBT), who are pregnant, who are under the age of 18 years, and who do not have comorbid depression and anxiety. Physicians should carefully consider the potential risks of implanting the Reclaim DBS System in patients with comorbid psychiatric disorders (e.g., bipolar, body dysmorphic, psychotic) as the Reclaim DBS System may aggravate the symptoms.

***Humanitarian Device:** The effectiveness of these devices for the treatment of dystonia and obsessive-compulsive disorder has not been demonstrated.

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