DBS EPILEPSY FACT SHEET

What is it?

The Medtronic Deep Brain Stimulation (DBS) System for Epilepsy is 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 1997, more than 150,000 patients worldwide have benefited from Medtronic DBS Therapy.[1]

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 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 surgery?

- 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.[3,4]
- 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.[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, quality of life, and neuropsychological measures of executive functions and attention. No significant cognitive declines or worsening of depression scores were observed through the blinded phase or at year 7. Long-term, there was an improvement in seizure frequency from baseline in patient subgroups whom had tried VNS or had a prior resective surgery.[4]
- 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.[2–5] 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.[2-5]

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

DBS Therapy for Epilepsy is an important addition 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 large randomized control trial.
- Unlike RNS, Medtronic DBS systems are MR Conditional and are safe for MRI scans under certain conditions.*
- Unlike RNS, Medtronic DBS therapy does not require the seizure foci to be identified for patients with focal (partial-onset) seizures.
- As many as 30% of patients that undergo an evaluation for resective surgery do not proceed to the procedure; therefore, alternative treatment options such as DBS are needed.

*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 at http://www.medtronic.com/us-en/c/dbs-unrivaled-commitment.html.

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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 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 and Precautions: 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 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. Tunneling the extension too superficially or too deeply may result in nerve or vascular injury, or tunneling through unintended anatomy. The lead-extension connector should not be placed in the soft tissues of the neck due to an increased incidence of lead fracture. 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. Loss of coordination in activities such as swimming may occur. 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.

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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References:

1. Data on file at Medtronic.
2. Fisher RS et al. Electrical stimulation of the anterior nucleus of thalamus for treatment of refractory epilepsy. *Epilepsia*. 2010 May; 51(5):899–908.
3. Salanova V et al. Long-term efficacy and safety of thalamic stimulation for drug-resistant partial epilepsy. *Neurology*. 2015 Mar10; 84(10):1017–25.
4. Sandok E et al. Long term outcomes of the SANTE Trial: 7-Year Follow-Up. American Epilepsy Society Annual Meeting. 2016 Abst. 1.298.
5. Tröster AI et al. Memory and mood outcomes after anterior thalamic stimulation for refractory partial epilepsy. *Seizure*. 2017 Feb; 45:133–141.
6. Dasheiff RM. Sudden unexpected death in epilepsy: a series from an epilepsy surgery program and speculation on the relationship to sudden cardiac death. *J Clin Neurophysiol*. 1991 8:216–222.

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