



New Study Shows Superiority of Intrathecal Baclofen Therapy (ITB Therapy(SM)) Over Oral Medication for the Treatment of Severe Post-Stroke Spasticity

January 11, 2018



Therapy Delivered via the Medtronic SynchroMed(TM) II Infusion System

DUBLIN - January 11, 2018 - Medtronic plc (NYSE:MDT) today announced the publication of results from the '[Spasticity In Stroke-Randomised Study \(SISTERS\) trial](#) in the *Journal of Neurology, Neurosurgery & Psychiatry* (JNNP). These results demonstrate the superiority of Medtronic ITB TherapySM with Lioresal[®]Intrathecal (baclofen injection) delivered via the SynchroMed(TM) II Infusion System compared to conventional medical management (CMM) for the reduction of severe post-stroke spasticity (PSS) in adults. The SynchroMed II Infusion System is the only system approved in the United States for ITB Therapy.

People suffering from severe spasticity have tight, stiff muscles that make it difficult to move or control their arms, legs, or body, which can make everyday activities exhausting and difficult. More than 12 million people worldwide suffer from spasticity.¹ PSS impacts up to 43 percent of patients in the first year after their stroke² and is considered severe when it interferes with comfort, function or caregiving, despite oral medications.³ Without effective treatment, the excessive muscle tone can cause pain and stiffness, deformity and reduced range of movement, significantly reducing overall quality of life.⁴

SISTERS is the first randomized, controlled, open-label, multicentre study to evaluate the efficacy and safety of ITB Therapy versus CMM with oral antispastic medications for treatment of PSS after six months' active treatment. Professor Leopold Saltuari, M.D., from the Tirol Clinic in Hochzirl, Austria, served as the coordinating investigator of the study, which randomized 60 patients in Europe and the United States. The primary outcome of the study was change in muscle tone and spastic hypertonia as measured by the change in average Ashworth scale (AS) score in the lower extremity (LE) of the affected body side from baseline to month six.⁵

Results of the study show ITB demonstrated a significant improvement over CMM in reducing muscle tone in the affected lower and upper extremities. On the 5-point AS scale, analysis showed mean AS score reduction for the affected lower extremity, -0.99 [ITB] vs. -0.43 [CMM] and for the affected upper extremity -0.66 [ITB] vs. -0.17 [CMM]. Functional change was evaluated using the Functional Improvement Measure (FIM). The ITB group demonstrated an improvement in FIM total score from baseline to month six (+2.68), while a worsening occurred in the CMM arm (-2.58).⁵

More patients reported adverse events in the ITB group (24/25 patients, 96 percent; 149 events) compared to CMM (22/35, 63 percent; 77 events), although events were generally consistent with the known safety profile of ITB Therapy. Around half of the drug, device and procedure related adverse events occurred during implant and titration phase. No patient discontinued ITB Therapy due to treatment related adverse events.⁵

"ITB Therapy is underused when it comes to treating severe spasticity in post-stroke patients," said lead author and study investigator Michael Creamer, D.O., of Central Florida Pain Relief Centers in Orlando, Fla. "The study results demonstrate that ITB Therapy is superior to oral medications in decreasing muscle tone." Dr. Creamer will be presenting the study results at the 21st North American Neuromodulation Society (NANS) Annual Meeting in Las Vegas on Saturday, January 13, 2018.

Stroke affects people all around the world regardless of gender, age or race. According to the World Health Organization, 15 million people suffer stroke worldwide each year, of these, 5 million are permanently disabled.⁶

"All over the world, PSS patients are suffering from inadequately managed severe spasticity that can interfere with their quality of life," said Charlie Covert, vice president and general manager, Targeted Drug Delivery, Medtronic Pain Therapies. "At Medtronic, we're committed to raising awareness of ITB Therapy as an effective treatment for severe PSS and to ensure it is available to the patients who need it most."

About ITB Therapy

ITB Therapy with Lioresal Intrathecal (baclofen injection) is indicated for use in the management of severe spasticity resulting from stroke, spinal cord injury, multiple sclerosis, cerebral palsy and brain injury. Patients should first respond to a screening dose of Lioresal Intrathecal prior to consideration for long term infusion via an implantable pump. For spasticity of spinal cord origin, ITB Therapy should be reserved for patients unresponsive to oral baclofen therapy, or those who experience intolerable CNS side effects at effective doses. Patients with spasticity due to traumatic brain injury should wait at least one year after the injury before consideration of long term ITB Therapy.

Abrupt discontinuation of intrathecal baclofen, regardless of the cause, has resulted in sequelae that include high fever, altered mental status, exaggerated rebound spasticity, and muscle rigidity, that in rare cases has advanced to rhabdomyolysis, multiple organ-system failure and death.

Prevention of abrupt discontinuation of intrathecal baclofen requires careful attention to programming and monitoring of the infusion system, refill scheduling and procedures, and pump alarms. Patients and caregivers should be advised of the importance of keeping scheduled refill visits and should be educated on the early symptoms of baclofen withdrawal. Special attention should be given to patients at apparent risk (e.g. spinal cord injuries at T-6 or above, communication difficulties, history of withdrawal symptoms from oral or intrathecal baclofen).

Consult the technical manual of the implantable infusion system for additional postimplant clinician and patient information (See

WARNINGS).

For important safety information, including BOX WARNING, refer to the [Lioresal Intrathecal \(baclofen injection\) prescribing information](#) and the [SynchroMed II Drug Infusion System Brief Statement](#).

About SynchroMedII Intrathecal Drug Delivery System

The Medtronic SynchroMed II pump and catheter are implanted under the skin and deliver medication into the intrathecal space, enabling clinicians to prescribe the lowest possible dose and tailor drug delivery to patient needs. Patients with chronic, intractable pain or severe spasticity who have not had success with other treatment options or have experienced intolerable side effects with oral medications are candidates for SynchroMedII. The system is also full-body MRI conditional under conditions specified in the product labeling. More than 375,000 patients worldwide have received therapy from Medtronic drug infusion systems since they were introduced over 30 years ago.⁷

About Medtronic

Medtronic plc (www.medtronic.com), headquartered in Dublin, Ireland, is among the world's largest medical technology, services and solutions companies - alleviating pain, restoring health and extending life for millions of people around the world. Medtronic employs more than 84,000 people worldwide, serving physicians, hospitals and patients in approximately 160 countries. The company is focused on collaborating with stakeholders around the world to take healthcare Further, Together.

Any forward-looking statements are subject to risks and uncertainties such as those described in Medtronic's periodic reports on file with the Securities and Exchange Commission. Actual results may differ materially from anticipated results.

Lioresal® is a registered trademark of Saol.

SynchroMed® is a registered trademark of Medtronic.

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Sources:

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