April 2002

IMPORTANT DRUG WARNING

Dear Healthcare Provider:

We have updated the prescribing information for Lioresal® Intrathecal (baclofen injection) to include a warning about rare cases of intrathecal baclofen withdrawal that can lead to life threatening sequelae and/or death in patients who abruptly discontinue therapy.

Lioresal Intrathecal is indicated for use in the management of severe spasticity of cerebral and spinal origin.

The following BOX WARNING has been added to the Lioresal Intrathecal prescribing information:

> 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.
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> Prevention of abrupt discontinuation of intrathecal baclofen requires careful attention to proper 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).

Additional details regarding the risk of baclofen withdrawal associated with Lioresal Intrathecal are included in the WARNINGS section of the prescribing information:

> ***Withdrawal:*** Abrupt withdrawal of intrathecal baclofen, regardless of the cause, has resulted in sequelae that included high fever, altered mental status, exaggerated rebound spasticity, and muscle rigidity that in rare cases progressed to rhabdomyolysis, multiple organ-system failure, and death. In the first 9 years of post-marketing experience, 27 cases of withdrawal temporally related to the cessation of baclofen therapy were reported; six patients died. In most cases, symptoms of withdrawal appeared within hours to a few days following interruption of baclofen therapy. Common reasons for abrupt interruption of intrathecal baclofen therapy included malfunction of the catheter (especially disconnection), low volume in the pump reservoir, and end of pump battery life; human error may have played a causal or contributing role in some cases. 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.
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> All patients receiving intrathecal baclofen therapy are potentially at risk for withdrawal. Early symptoms of baclofen withdrawal may include return of baseline spasticity, pruritus,

hypotension, and paresthesias. Some clinical characteristics of the advanced intrathecal baclofen withdrawal syndrome may resemble autonomic dysreflexia, infection (sepsis), malignant hyperthermia, neuroleptic-malignant syndrome, or other conditions associated with a hypermetabolic state or widespread rhabdomyolysis.

Rapid, accurate diagnosis and treatment in an emergency-room or intensive-care setting are important in order to prevent the potentially life-threatening central nervous system and systemic effects of intrathecal baclofen withdrawal. The suggested treatment for intrathecal baclofen withdrawal is the restoration of intrathecal baclofen at or near the same dosage as before therapy was interrupted. However, if restoration of intrathecal delivery is delayed, treatment with GABA-ergic agonist drugs such as oral or enteral baclofen, or oral, enteral, or intravenous benzodiazepines may prevent potentially fatal sequelae. Oral or enteral baclofen alone should not be relied upon to halt the progression of intrathecal baclofen withdrawal.

Seizures have been reported during overdose and with withdrawal from LIORESAL INTRATHECAL as well as in patients maintained on therapeutic doses of LIORESAL INTRATHECAL.

In addition, we have enclosed a copy of the updated Emergency Procedure Card for both intrathecal baclofen underdose/withdrawal and for intrathecal baclofen overdose.

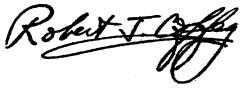
Please refer to the enclosed Lioresal Intrathecal (baclofen injection) Package Insert for full prescribing information.

Healthcare professionals are strongly encouraged to report any serious adverse events that occur with the use of Lioresal Intrathecal to Medtronic at 1.800.328.0810 or to the FDA's MedWatch program by phone (1-800-FDA-1088), fax (1-800-FDA-0178), via the MedWatch website at www.FDA.gov/medwatch, or by mail (using postage-paid form) to MedWatch, HF-2, 5600 Fishers Lane, Rockville, MD 208572-9787.

If you have any questions regarding Lioresal Intrathecal, please contact Medtronic Neurological Technical Services at 1.800.707.0933

Sincerely,

Medtronic, Inc.



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