



Medtronic

ITB TherapySM

FOR PEOPLE SEEKING RELIEF
OF SEVERE SPASTICITY



RELEASE
your potential



Medtronic



*Andrina M.
Living with cerebral palsy
Receiving ITB Therapy since 2007*

Discover ITB Therapy

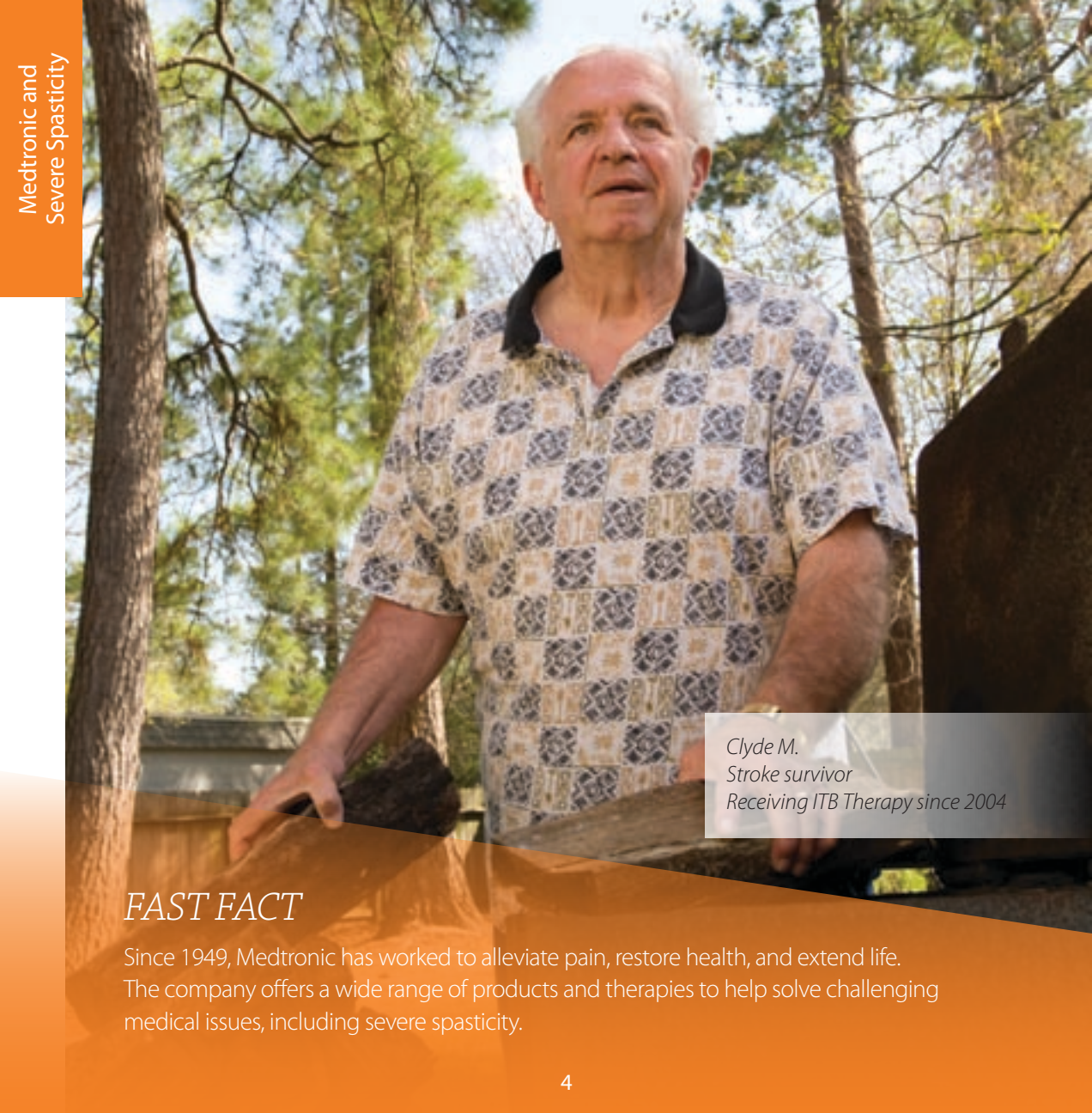
Imagine living comfortably with severe spasticity. Everyday activities like brushing your hair, tying your shoelaces, walking, getting in and out of a car, eating a meal, and sleeping peacefully might be easier, more pleasurable. You may be able to rethink what you can achieve, to set goals and pursue opportunities that interest you. It may be possible, when spasticity is controlled.

Spasticity occurs when there is injury to a part of the central nervous system (the brain or spinal cord) that controls voluntary movements. The damage causes a change in the balance of signals between the nervous system and muscles, and can cause spasticity or spasms. Cerebral palsy, brain injury, stroke, multiple sclerosis, and spinal cord injury are some of the conditions associated with spasticity.

For the management of severe spasticity, Medtronic offers ITB TherapySM (intrathecal baclofen therapy) delivered through the Medtronic SynchroMed[®] II programmable drug delivery system (sometimes referred to as the baclofen pump). Since 1992, more than 50,000 Medtronic baclofen pumps have helped individuals with severe spasticity. With looser muscles, those receiving the therapy may move more freely, experience less spasticity-related pain, have more confidence, and feel less limited in their abilities.

While there are currently no cures for the underlying conditions that cause spasticity, ITB Therapy is reversible and can be removed if other treatment options—or even cures—become available. For now, ITB Therapy offers hope for release from spasticity and its control over your life. As you consider these possible benefits, you should also explore the risks of treatment. This booklet discusses the benefits, risks, and side effects associated with ITB Therapy. The therapy is not for everyone.

Imagine how greater control of spasticity might positively affect your life. Begin your exploration of ITB Therapy in the following pages.



*Clyde M.
Stroke survivor
Receiving ITB Therapy since 2004*

FAST FACT

Since 1949, Medtronic has worked to alleviate pain, restore health, and extend life. The company offers a wide range of products and therapies to help solve challenging medical issues, including severe spasticity.

Expand Your Possibilities with ITB Therapy

Many people have found that loosening spasticity's grip allows them to enjoy simple activities that previously were complicated for them. What might this release mean for you? It may result in less spasticity-related pain. You may be able to transfer between sitting and standing more easily, climb stairs, brush teeth, bathe, or walk with greater ease.

A common treatment for spasticity is oral medication (pills). One medication for spasticity is a muscle relaxer called baclofen. Although oral baclofen works for many people, some may need high doses to manage their spasticity. A high level of drug in your body can cause side effects such as weakness, drowsiness, nausea, or other negative effects, and still may not provide the desired results.

How It Works

If you continue to experience side effects or your spasticity is not well controlled with oral baclofen, ITB Therapy may be the right choice for you. ITB Therapy uses baclofen but delivers it in a liquid form called Lioresal® Intrathecal (baclofen injection).

The medicine is delivered directly into the fluid-filled area surrounding the spinal cord, called the intrathecal space, using a programmable pump that is surgically placed inside your body. When pills are taken by mouth, the medication enters the bloodstream and then crosses the fluid that surrounds the brain and spinal cord. Since Lioresal Intrathecal goes directly into the fluid around your spinal cord, you may need a fraction of the oral medication dose.¹ Administration of intrathecal baclofen may still have undesirable side effects but because a lower dose of the drug may be used, the side effects may not be as pronounced as with oral baclofen.

ITB Therapy works by using the Medtronic SynchroMed II infusion system which includes:

- **A programmable drug pump**—A battery-powered device that stores and dispenses medicine according to instructions programmed by your clinician

- **Surgically placed catheter**—A thin, flexible tube that connects to the pump and delivers medication from the pump to the area where fluid flows around the spinal cord

The SynchroMed II system is surgically placed just under the skin of the abdomen. Most people report that it is not uncomfortable or restrictive and does not interfere with their movements.

Releasing Spasticity

Studies show that ITB Therapy may reduce spasticity²⁻¹⁰ and spasms,^{3,4,9,10} potentially allowing you greater ability to perform activities of daily living.¹¹⁻¹⁴ Releasing spasticity may expand possibilities for you in small and significant ways. You may feel that you have control over spasticity rather than it controlling you, and that your goals and aspirations are more within reach.

ITB Therapy is approved by the FDA and is covered by most private health insurance companies, Medicare, and most state Medicaid programs.

FAST FACT

Your clinician programs your SynchroMed pump to manage your muscle tone throughout the day. For example, it can be set to deliver less medication in the daytime when you may rely on your stiffness to walk, transfer, or put on clothes, then automatically deliver more medication at night to reduce spasticity to help you sleep.

Is ITB Therapy Right for You?

Determining if You Are a Candidate

One important benefit of ITB Therapy is that you can try it first during a screening test before you commit to long-term therapy. It is an opportunity to see how your body will react to ITB Therapy. Your experience during the screening test will be used by you and your clinician to decide if long-term therapy is right for you.

ITB Therapy might be the right choice if you have:

- severe spasticity as a result of injuries or events to the brain or spinal cord.
- sufficient body size (based on your height and weight) to support the pump.
- a spinal cord injury or disease and experience ineffective results or side effects (such as fatigue or nausea) from oral medications.
- a traumatic brain injury and it has been at least 1 year since your injury.

In addition, ITB Therapy may also be considered if you experience one or more of the following:

- Severe spasticity or spasms that interfere with function or your daily activities
- Severe spasticity or spasms that interfere with your care or positioning
- Severe spasticity causing spasticity-related pain

ITB Therapy is not recommended if you have:

- an infection at the time of the surgical procedure to place the infusion system.
- history of allergy (hypersensitivity) to oral baclofen.

Talk with your physician about ITB Therapy. If your physician recommends it, you will be asked to schedule a screening test as a next step to determine how you may respond to ITB Therapy.

Move Forward

A Screening Test Is the First Step

The screening test is the first step in determining if ITB Therapy will work for managing your spasticity. The purpose of the screening test is to see if you respond to a small, temporary dose of intrathecal baclofen.

Many compare the screening test to a light switch—either it is completely “on” or entirely “off.” Long-term ITB Therapy is similar to a dimmer switch that allows for different levels of brightness. After you begin receiving ITB Therapy, the medication can be adjusted to the precise amount needed so you are not too loose or too tight.

A Test Dose

During the screening test, your clinician will inject a small dose of Lioresal Intrathecal into the intrathecal space (where fluid flows around your spinal cord). It may be performed in a hospital or surgery center. Your response to the medicine will be monitored during the screening.

The medication may take 30 minutes to 1 hour to relax your muscles. You might feel the greatest effect about 4 hours after the injection, and the effect typically lasts 4 to 8 hours. After the medication wears off, you will return to the same amount of spasticity you had prior to the test.

In clinical studies, a positive response to the screening test was demonstrated in:

- 97% of patients with spasticity related to the spine¹⁰
- 86% of patients with spasticity related to the brain¹⁵

Everyone Responds Differently

It is important to note that everyone responds differently to the test dose. During the screening test, your muscles may loosen only slightly, or your muscles might feel so

completely loose or weak that you can't use them, especially your legs. If your muscles become overly loose or "noodly," remember that this is temporary. Either response simply means that ITB Therapy may work for you. Once you begin receiving ITB Therapy, you will work closely with your clinician to adjust the medication to meet your needs.

During the screening test, these temporary side effects are possible:

- Overly loose muscles
- Headache
- Sleepiness
- Dizziness
- Nausea/vomiting

Be sure to tell your clinician if you experience any of these possible side effects.

After your screening test, you and your clinician will discuss your results and determine if you are a candidate for ITB Therapy. You must have a positive screening test to move forward with ITB Therapy.

FAST FACT

Sometimes people don't respond to the first test dose of medication. If this happens, your clinician may give you a second test dose using the same procedure and a larger amount of medication. If this still does not loosen your muscles, your clinician may give you an even larger dose. If this dose does not loosen your muscles, you are not a candidate for ITB Therapy.



Ariel F.
Living with brain injury
Receiving ITB Therapy since 2007

“Ariel had to have his pump removed due to a complication. It was a couple of weeks before Christmas, and one day Ariel was crying due to the pain in his leg and the increased amount of spasticity. He looked at me with tears in his eyes and said, ‘Mom, all I want for Christmas is my pump.’”

– Ana C., Ariel’s mother

Reach to Achieve

Goal Setting with Your Clinician

Receiving ITB Therapy has the potential to be a new beginning for you by relieving the spasticity that prevents you from using your abilities. It may help you unlock your potential. As you consider ITB Therapy, think about the types of activities you would like to pursue with the help of this therapy.

In at least four studies, the therapy has helped people become more independent, allowing them to perform activities of daily living including feeding or dressing themselves, sitting more comfortably, or transferring more easily.^{11-13,16} Imagine the great difference these important achievements can make in your daily life.

You can set goals for each phase of your ITB Therapy experience, beginning with the screening test and continuing after you begin receiving the therapy. For example, a screening test goal may be to bend an arm or leg that has been stiff due to spasticity. A goal for long-term ITB Therapy may be to get in and out of the bathtub more easily.

Talk with your clinician about the activities that may be possible for you with ITB Therapy, and record them below. What would you like to try? What would you like to achieve? How might physical therapy help? Share your goals with your friends and family and celebrate your accomplishments. Release your potential with ITB Therapy.

- My goals for the screening test:

- My goals for ITB Therapy:

- Life goals that may be possible with ITB Therapy:

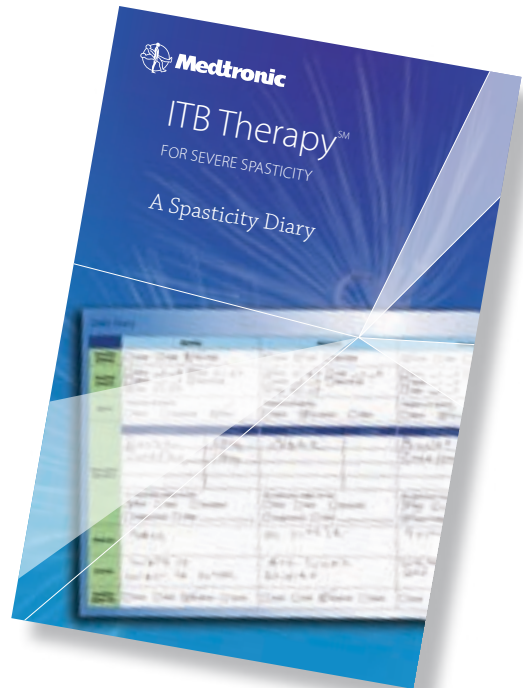
- Feedback from my doctor about my goals:

Tracking Spasticity

Monitoring Your Condition

The nature of spasticity is that it changes—periods of loose muscles can be followed by painful spasms. Your spasticity may be different from day to day or hour to hour.

A daily diary can help you and your clinician determine what times of day and which days of the week spasticity is most troublesome for you. A pattern may emerge that responds well to ITB Therapy, and this information will help identify programming parameters and dosing needs. The SynchroMed II pump programming features allow it to dispense more medication at different times of the day and different days of the week so you can be looser or tighter depending on your needs.



See a sample of a Spasticity Diary on the next page. You can print these diary pages at www.spasticity.com/diary. Complete these sheets for several days and share them with your clinician.

Sample Spasticity Diary

The sample diary chart below shows *Morning* and *Afternoon* entry columns. (Note: The *Evening* and *Overnight* columns are not shown here, but are included in the sample diary available online for download and printing.)

	Morning		Afternoon	
Spasticity Intensity	<input type="checkbox"/> Loose <input type="checkbox"/> Tight <input type="checkbox"/> Very Tight		<input type="checkbox"/> Loose <input type="checkbox"/> Tight <input type="checkbox"/> Very Tight	
Spasticity Location	<input type="checkbox"/> Arms: ___ L ___ R <input type="checkbox"/> Feet: ___ L ___ R <input type="checkbox"/> Hands: ___ L ___ R <input type="checkbox"/> Neck/Trunk <input type="checkbox"/> Legs: ___ L ___ R		<input type="checkbox"/> Arms: ___ L ___ R <input type="checkbox"/> Feet: ___ L ___ R <input type="checkbox"/> Hands: ___ L ___ R <input type="checkbox"/> Neck/Trunk <input type="checkbox"/> Legs: ___ L ___ R	
Spasms	Frequency of spasms: <input type="checkbox"/> None <input type="checkbox"/> Occasional <input type="checkbox"/> Often		Frequency of spasms: <input type="checkbox"/> None <input type="checkbox"/> Occasional <input type="checkbox"/> Often	
Medications/ Side Effects	Medications		Medications	
	Dosages		Dosages	
	My medication makes me feel: <input type="checkbox"/> Tired <input type="checkbox"/> Alert <input type="checkbox"/> Nauseated <input type="checkbox"/> Foggy/cloudy <input type="checkbox"/> Other: _____		My medication makes me feel: <input type="checkbox"/> Tired <input type="checkbox"/> Alert <input type="checkbox"/> Nauseated <input type="checkbox"/> Foggy/cloudy <input type="checkbox"/> Other: _____	
Weakness				
Activities				
Spasticity-related Pain	<input type="checkbox"/> None <input type="checkbox"/> Mild <input type="checkbox"/> Moderate <input type="checkbox"/> Severe		<input type="checkbox"/> None <input type="checkbox"/> Mild <input type="checkbox"/> Moderate <input type="checkbox"/> Severe	

Studying the Benefits

It may be comforting to know that ITB Therapy has been studied since 1984. Many people have experienced—and studies have confirmed—improvement in spasticity with Medtronic ITB Therapy. With spasticity released, people are better able to embrace new opportunities. The information below will provide you with a summary of benefits identified in a number of studies.

ITB Therapy is approved for people who have severe spasticity as a result of injuries or events affecting the brain or spinal cord. It has been studied in people who have cerebral palsy, stroke, brain injury, spinal cord injury, and multiple sclerosis. Studies have shown that many people have benefited from ITB Therapy in the following ways:

- Significantly reduced spasticity²⁻¹⁰ and spasms^{3,4,9,10}
- Increased independence allowing people to better perform activities of daily living including feeding or dressing themselves, sitting more comfortably, or transferring more easily¹¹⁻¹⁴

A significant number of caregivers also find satisfaction with ITB Therapy.^{13,17}

Research Studies Summary

Following is a summary of some of the research studies behind ITB Therapy.

Spasticity Related to the Brain (e.g., cerebral palsy, brain injury, or stroke)

ITB Therapy:

- may provide long-term control of spasticity in people living with cerebral palsy or brain injury according to a study.²
- reduces spasticity in both the arms and legs of those living with cerebral palsy, brain injury, and stroke.^{6-8, 18,19}

For people with cerebral palsy, ITB Therapy may:

- slow or prevent the development of hip problems according to a study.²⁰
- delay or avoid orthopedic surgery as shown in another study.²¹

For stroke survivors, ITB Therapy may:

- have no effect on the side of the body that was not affected by the stroke according to two studies.^{6,7}
- provide improvement in function and quality of life according to a study.⁶
- result in improved walking speed as shown in another study.⁵

For people with brain injury, ITB Therapy may:

- improve cleanliness and transfer scores (your ability to be moved to a bed or wheelchair) as revealed in a study.²²

Spasticity Related to the Spine

(e.g., multiple sclerosis or spinal cord injury)

ITB Therapy may:

- provide long-term control of spasticity according to a study.¹⁰
- result in improved function as shown in a second study.²³
- improve bowel and bladder performance for individuals with spinal cord injury according to another study.²⁴

If you have multiple sclerosis, one study shows timely management of severe spasticity may help you maintain your ability to walk.²⁵

Understanding the Risks

When considering ITB Therapy, it is important to be familiar with both the benefits and the risks. The risks associated with the therapy are outlined below.

Important Safety Information on ITB Therapy:

Please follow your doctor's instruction closely because a sudden stop of intrathecal baclofen therapy can result in serious illness such as high fever, changed mental status, muscle rigidity, and in rare cases multiple organ-system failure and death. It is very important that your doctor be called right away if you experience any of these symptoms. It is important for you to keep your scheduled refill visits so you don't run out of Lioresal Intrathecal and to understand the early symptoms of baclofen withdrawal. Some people are at more risk than others for baclofen withdrawal; consult with your doctor.

Side effects associated with ITB Therapy usually are temporary and can be managed by adjusting the dosage of Lioresal Intrathecal in the pump.

The most common side effects include:

- Loose muscles
- Sleepiness
- Upset stomach
- Nausea/vomiting
- Headache
- Dizziness

Pump or catheter failure may cause an overdose (too much medication) or underdose (too little medication) of intrathecal baclofen. The signs and symptoms of an overdose include:

- Drowsiness
- Lightheadedness
- Loss of consciousness or coma
- Seizures
- Difficulty breathing

The signs and symptoms of an underdose include:

- Itching
- Low blood pressure
- Increase or return of spasticity
- Lightheadedness
- Tingling sensation

The following are possible complications:

- The catheter or pump could move within the body
- The pump could stop because the battery has run out or because of mechanical failure
- The catheter could leak, tear, kink, or become disconnected resulting in an underdose or abrupt stop of intrathecal baclofen; an abrupt stop of Lioresal Intrathecal can lead to:
 - High fever
 - Altered mental status
 - Returned spasticity
 - Muscle stiffness
 - Death, in rare cases

Talk with your clinician about any additional side effects or complications associated with your treatment.

If you decide to receive ITB Therapy, you will need to inform a health care professional that you have ITB Therapy before any medical or diagnostic procedure (e.g., MRI, diathermy).

If you or your clinician have questions regarding your pump and a medical or diagnostic procedure, please call Medtronic Neuromodulation Patient Services at 800-510-6735, Monday through Friday, 8:00 am to 5:00 pm Central Time.

For more information, please read the Lioresal Intrathecal Patient Information and the SynchroMed infusion system brief summary located at the back of this booklet.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

The Procedure and Afterward

If your screening test is successful and you and your doctor agree to pursue ITB Therapy, the next step is to implant the Medtronic SynchroMed infusion system that will provide long-term treatment. ITB Therapy has helped thousands of individuals release their spasticity, giving them the opportunity to enjoy the simple pleasures in everyday life.

The Procedure for ITB Therapy

Before the surgery, you and your doctor will decide where to position the baclofen pump for your comfort. The SynchroMed II pump is implanted during a surgical procedure that takes approximately 1 to 3 hours and requires a brief hospital stay.

During the surgical procedure, the doctor will form a pocket under the skin that is large enough to hold the pump.



The Procedure
and After

*SynchroMed® II
programmable pump
with catheter
(Actual size)*

This pocket is placed in the abdomen. A second incision is made on the back, where one end of the catheter will be placed in the fluid-filled area surrounding the spinal cord. The other end of the catheter is attached to the pump resulting in a fully implanted system. Once the pump and catheter are in place, the incisions are closed and the surgery is complete. The length of your hospital stay will vary depending on your physician's preference and your insurance policies.

After the Procedure

After surgery, there may be some discomfort and tenderness where your pump and catheter are placed. This is a natural part of the healing process. Your clinician may prescribe medication to relieve the pain from surgery.

Your clinician may recommend that you limit activity for 6 to 8 weeks after surgery.

As you heal, take time to make plans for returning to the activities you like. Discuss your goals with your clinician and loved ones, and develop a plan for doing the things that matter most to you. Setting goals will help you get the most out of ITB Therapy.

To achieve these goals, you may need physical therapy or other forms of rehabilitation. While ITB Therapy may help control your spasticity and spasms, rehabilitation may address any weakness, loss of motor control, or lack of endurance you may experience. Spasticity management and neurorehabilitation are intertwined, and should be addressed together to improve function and work toward your goals.

Optimal Dosing

Your clinician will adjust the pump to manage your spasticity by delivering the dose of medication that's just right for you. It may take several weeks or months to reach your optimal dose. You will receive information on recognizing signs of underdose or overdose of medicine in your pump so you can alert your clinician promptly since these may result in serious medical problems.

Your clinician will determine if you still need to take other medications after receiving ITB Therapy.

Follow-up Care

One of your most important responsibilities is to make regular return visits to your clinic to ensure ongoing therapy. It is important to attend all of your refill visits and maintain some level of medicine in your pump. If your pump runs out of medication, you will abruptly stop receiving intrathecal baclofen; this can result in serious medical problems, and in rare cases has been fatal.

On average, a refill appointment lasts 35 to 45 minutes. During a typical follow-up visit, your clinician will refill your pump and check your system to make sure you are receiving the most appropriate therapy. The pump is refilled by inserting a needle through your skin and injecting new medication into your pump. This usually is a painless procedure.

For more information, please refer to the Lioresal Intrathecal patient information and the SynchoMed II infusion system brief summary located at the back of this brochure.

FAST FACT

Your pump should only be filled with intrathecal baclofen that has been approved by the FDA. This form of baclofen is called Lioresal Intrathecal. You are encouraged to ask your clinician for Lioresal Intrathecal when your pump is refilled. There currently is no generic equivalent for this medication. This means that if you are not receiving Lioresal Intrathecal, you are not getting the medication approved for use with ITB Therapy.



“ITB Therapy isn’t saving my life, but it helps me live my life without worrying about my disability. In a sense, that is saving my life.”

– Jason F., living with spinal cord injury, receiving ITB Therapy since 1991

The Support You Need

When you choose Medtronic ITB Therapy, you have the confidence that comes with knowing your therapy has been thoroughly studied and monitored. You are supported by a worldwide network of clinicians and Medtronic representatives who ensure you have the care you need, no matter where life takes you.

At Medtronic, we are committed to bringing together technology, people, and programs to improve lives.

For more information on ITB Therapy:

- visit www.spasticity.com or call 1-800-856-3823.
- talk with your clinician about ITB Therapy.

Talk with Someone Receiving ITB Therapy

It may be helpful for you to talk with someone who is receiving ITB Therapy to help control severe spasticity. Medtronic has volunteer ambassadors who are eager to share their stories and experiences and answer your questions.

To participate:

- Call 800-503-4110. Phones are staffed from Monday through Friday, 7:00 am to 6:00 pm Central Time. You can also visit www.spasticity.com/ambassador 24 hours a day.
- You will be asked a few questions to help pair you with an ambassador whose situation is similar to your own. Then your name and phone number will be shared with your ambassador.
- Your ambassador will call you at a convenient time for you and will share his or her personal experience with ITB Therapy.

Be Curious

Talk With Your Clinician

When considering ITB Therapy, it is important to talk candidly with your clinician about the treatment and to ask questions. Following is a list of questions for every stage of your decision-making process. Circle the questions you want to ask your clinician, then take this list with you to your appointments to help guide the conversation.

Considerations

- What treatments are used to manage severe spasticity? What are my options?
- Is ITB Therapy a possible treatment for me?
- What are possible treatment goals for me?

Expectations

- What results have you seen with ITB Therapy? What should I expect?
- What happens during the screening test?
- What should I expect on the day of my surgery? How much time should I expect to spend in the hospital?
- Where will the pump be placed?
- How long will it take for my severe spasticity to improve?

Daily Living

- Will ITB Therapy improve my comfort or ability to perform activities of daily living?
- How might ITB Therapy affect work, travel, recreation, sexual activity, and exercise?
- Are there any physical activities I would need to avoid?
- Will the pump interfere with medical procedures? If so, which procedures?
- If I became pregnant, how would that affect the therapy?
- Is the pump affected by electromagnetic interference (EMI), heat, pressure changes, or magnets?



“With ITB Therapy, you can do most anything that you want to do. You just have to figure out how to do it, and you might have to figure out how to do it in a different way.”

– Cindy H., living with multiple sclerosis, receiving ITB Therapy since 1996

Physical Therapy

- Would I need physical or occupational therapy? If so, what type of therapy?
- What might physical or occupational therapy do for me?

Benefits and Risks

- What are the risks and potential benefits of ITB Therapy?

Drug Choice

- Are there medications that must be avoided while receiving ITB Therapy? Can my current prescriptions be used with ITB Therapy?
- What are the differences between compounded (pharmacy manufactured or mixed) intrathecal baclofen and commercially available medicine, such as Lioresal Intrathecal?
- What type of drug would I receive in my pump? Lioresal Intrathecal or a compounded medication?

Achieving the Right Dosage

- How often would my dose need to be adjusted, and when can I expect to reach my target dose?

Refills

- How would the therapy be monitored, and how often would I need to have my pump refilled?
- What happens when the pump is refilled?

Overdose/Underdose

- What are the signs and symptoms of baclofen overdose (too much medication) and underdose (too little medication)? What would I do if I experience any of these symptoms?

Pump Mechanics

- How long does the pump's battery typically last?

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Visit us at www.spasticity.com for more information on ITB Therapy, including personal experiences with this treatment, information on contacting an ITB Therapy ambassador, and assistance locating a doctor.

SYNCHROMED® II DRUG INFUSION SYSTEM BRIEF SUMMARY:

Product technical manuals and the appropriate drug labeling must be reviewed prior to use for detailed disclosure.

Indications:

US: Chronic intraspinal (epidural and intrathecal) infusion of preservative-free morphine sulfate sterile solution in the treatment of chronic intractable pain, chronic intrathecal infusion of preservative-free ziconotide sterile solution for the management of severe chronic pain, and chronic intrathecal infusion of Lioresal® Intrathecal (baclofen injection) for the management of severe spasticity; chronic intravascular infusion of flouxiridine (FUDR) and methotrexate for the treatment of primary or metastatic cancer. Outside of US: Chronic infusion of drugs or fluids tested as compatible and listed in the product labeling.

Contraindications:

Infection; implant depth greater than 2.5 cm below skin; insufficient body size; spinal anomalies; drugs with preservatives, drug contraindications, drug formulations with pH < 3, use of catheter access port (CAP) kit for refills or of refill kit for catheter access, blood sampling through CAP in vascular applications, use of Personal Therapy Manager to administer opioid to opioid-naïve patients or to administer ziconotide.

Warnings:

Non-indicated formulations may contain neurotoxic preservatives, antimicrobials, or antioxidants, or may be incompatible with and damage the system. Failure to comply with all product instructions, including use of drugs or fluids not indicated for use with system, or of questionable sterility or quality, or use of non-Medtronic components or inappropriate kits, can result in improper use, technical errors, increased risks to patient, tissue damage, damage to the system requiring revision or replacement, and/or change in therapy, and may result in additional surgical procedures, a return of underlying symptoms, and/or a clinically significant or fatal drug under- or overdose. Refer to appropriate drug labeling for indications, contraindications, warnings, precautions, dosage and administration information, screening procedures and underdose and overdose symptoms and methods of management. Physicians must be familiar with the drug stability information in the product technical manuals and must understand the dose relationship to drug concentration and pump flow rate before prescribing pump infusion. Implantation and ongoing system management must be performed by individuals trained in the operation and handling of the infusion system. An inflammatory mass that can result in serious neurological impairment, including paralysis, may occur at the tip of the implanted catheter. Clinicians should monitor patients on intraspinal therapy carefully for any new neurological signs or symptoms, change in underlying symptoms, or need for rapid dose escalation.

Inform patients of the signs and symptoms of drug under- or overdose, appropriate drug warnings and precautions regarding drug interactions, potential side effects, and signs and symptoms that require medical attention, including prodromal signs and symptoms of inflammatory mass. Failure to recognize signs and symptoms and seek appropriate medical intervention can result in serious injury or death. Instruct patients to notify their healthcare professionals of the implanted pump before medical tests/procedures, to return for refills at prescribed times, to carry their Medtronic device identification card, to avoid manipulating the pump through the skin, to consult with their clinician if the pump alarms and before traveling or engaging in activities that can stress the infusion system or involve pressure or temperature changes. Strong sources of electromagnetic interference (EMI), such as short wave (RF) diathermy and MRI, can negatively interact with the pump and cause heating of the implanted pump, system damage, or changes in pump operation or flow rate, that can result in patient injury from tissue heating, additional surgical procedures, a return of underlying symptoms, and/or a clinically significant or fatal drug underdose or overdose. Avoid using shortwave (RF) diathermy within 30 cm of the pump or catheter. Effects of other types of diathermy (microwave, ultrasonic, etc.) on the pump are unknown. Drug infusion is suspended during MRI; for patients who can not safely tolerate suspension, use alternative drug delivery method during MRI. Patients receiving intrathecal baclofen therapy are at higher risk for adverse events, as baclofen withdrawal can lead to a life threatening condition if not treated promptly and effectively. Confirm pump status before and after MRI. Reference product labeling for information on sources of EMI, effects on patient and system, and steps to reduce risks from EMI.

Precautions:

Monitor patients after device or catheter replacement for signs of underdose/overdose. Infuse preservative-free (intraspinal) saline or, for vascular applications, infuse heparinized solutions therapy at minimum flow rate if therapy is discontinued for an extended period of time to avoid system damage. EMI may interfere with programmer telemetry during pump programming sessions. EMI from the SynchroMed programmer may interfere with other active implanted devices (e.g., pacemaker, defibrillator, neurostimulator).

Adverse Events:

Include, but are not limited to, spinal/vascular procedure risks; infection; bleeding; tissue damage, damage to the system or loss of, or change in, therapy that may result in additional surgical procedures, a return of underlying symptoms, and/or a clinically significant or fatal drug underdose or overdose, due to end of device service life, failure of the catheter, pump or other system component, pump inversion, technical/programming errors, or improper use, including use of non-indicated formulations and/or not using drugs or system in accordance with labeling; pocket seroma, hematoma, erosion, infection; post-lumbar puncture (spinal headache); CSF leak and rare central nervous system pressure-related problems; hygroma; radiculitis; arachnoiditis; spinal cord bleeding/damage; meningitis; neurological impairment (including paralysis) due to inflammatory mass; potential serious adverse effects from catheter fragments in intrathecal space, including potential to compromise antibiotic effectiveness for CSF infection; anesthesia complications; body rejection phenomena; local and systemic drug toxicity and related side effects; potential serious adverse effects from catheter placement in intravascular applications.

USA Rx Only Rev 0809

Patient Information

LIORESAL® INTRATHECAL (baclofen injection 40 mg/20 mL, 10 mg/5 mL, 10 mg/20 mL, 0.05 mg/1 mL)

Completely read this information before you start using Medtronic ITB TherapySM (Intrathecal Baclofen Therapy). This information does not take the place of thorough discussions with your doctor. You and your doctor should discuss ITB Therapy before you begin receiving the therapy and at regular refill appointments.

Q: What is Lioresal® Intrathecal (baclofen injection)?

A: Lioresal Intrathecal is a liquid form of baclofen, and is commonly used to treat severe spasticity. Liquid baclofen is used for injections and infusion into the intrathecal space (the fluid-filled area surrounding the spinal cord), using an implantable drug delivery system.

Q: What is severe spasticity?

A: Severe spasticity is tight, stiff muscles that make movements – especially of the arms and legs – difficult or uncontrollable. Severe spasticity can interfere with an individual's function and/or comfort.

Q: Who is a candidate for Lioresal Intrathecal?

A: People who suffer from severe spasticity resulting from cerebral palsy, multiple sclerosis, stroke, traumatic brain injury, or spinal cord injury, and who suffer intolerable side effects from oral baclofen (pills), may be a candidate for Lioresal Intrathecal. A screening test will help determine if you will respond to the intrathecal medication. Talk with your doctor about whether Lioresal Intrathecal may be an option for you.

Q: Who is not a candidate for Lioresal Intrathecal?

A: People who are hypersensitive (extremely sensitive) to oral baclofen should not take Lioresal Intrathecal.

Q: What are the most common side effects of Lioresal Intrathecal?

A: The side effects of intrathecal baclofen include loose muscles, sleepiness, upset stomach, vomiting, headaches, and dizziness. As with most medications, overdose (drug dose is too high) or under dose (drug dose is too low) can occur. Talk with your doctor about the side effects you may experience from your treatment.

Q: What do I need to know if I am using Lioresal Intrathecal?

A: Abruptly stopping intrathecal baclofen can result in serious medical problems and in rare cases has been fatal. It is important to keep your pump filled with medication by attending regularly scheduled refill appointments.

Q: What are the signs of rapid or abrupt withdrawal from intrathecal baclofen?

A: Increase or return in spasticity, itching, low blood pressure, lightheadedness, and tingling sensation are often early indications of baclofen withdrawal. It is very important that your doctor be called right away if you experience any of the above symptoms. In rare cases, severe symptoms may occur. These symptoms include high fever, altered mental status, spasticity worse than before you started ITB Therapy, and muscle rigidity. It is very important that your doctor be called right away if you experience any of the above symptoms.

Q: What can I do to prevent baclofen underdose or abrupt discontinuation of intrathecal baclofen?

A: It is very important that you keep all of your refill appointments. This may require some planning prior to traveling. Maintaining a regular refill schedule will ensure the pump does not run out of medication and that any potential problems with the infusion system are diagnosed and corrected. Additionally, you should be aware of what your pump alarms sound like. If you hear an alarm, contact your doctor immediately. Furthermore, it is very important that you know and understand the signs of baclofen underdose. Also be sure to tell your doctor right away if you experience any unusual symptoms, side effects, or changes in your condition.

Q: What are the symptoms of baclofen overdose?

A: Although rare, it is possible for you to receive too much medication (overdose). A baclofen overdose may cause drowsiness, lightheadedness, respiratory depression (difficulty breathing), seizures, loss of consciousness and coma. If you experience any of the above symptoms, it is very important that you or your caregiver contact your doctor right away.

This provides a summary of the most important information about Lioresal Intrathecal. If you would like more information, talk with your doctor. You can ask for information about Lioresal Intrathecal that is written for healthcare professionals. You also can get more information by visiting www.spasticity.com.

Rx only. Rev 0809

Lioresal® is a registered trademark of Novartis Pharmaceuticals Corporation.

www.medtronic.com

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Minneapolis, MN 55432-5604
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Toll-free 1-800-328-0810



Lioresal® Intrathecal (baclofen injection) Package Insert

If missing, please visit www.spasticity.com
and select Important Safety Information.

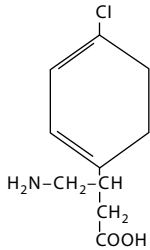
LIORESAL® INTRATHECAL

(baclofen injection)

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)

DESCRIPTION

LIORESAL INTRATHECAL (baclofen injection) is a muscle relaxant and antispastic. Its chemical name is 4- amino- 3-(4- chlorophenyl) butanoic acid, and its structural formula is:



Baclofen is a white to off-white, odorless or practically odorless crystalline powder, with a molecular weight of 213.66. It is slightly soluble in water, very slightly soluble in methanol, and insoluble in chloroform.

LIORESAL INTRATHECAL is a sterile, pyrogen-free, isotonic solution free of antioxidants, preservatives or other potentially neurotoxic additives indicated only for intrathecal administration. The drug is stable in solution at 37° C and compatible with CSF. Each milliliter of LIORESAL INTRATHECAL contains baclofen U. S. P. 50 mcg, 500 mcg or 2000 mcg and sodium chloride 9 mg in Water for Injection; pH range is 5.0 - 7.0. Each ampule is intended for SINGLE USE ONLY. Discard any unused portion. **DO NOT AUTOCLAVE**

CLINICAL PHARMACOLOGY

The precise mechanism of action of baclofen as a muscle relaxant and antispasticity agent is not fully understood. Baclofen inhibits both monosynaptic and polysynaptic reflexes at the spinal level, possibly by decreasing excitatory neurotransmitter release from primary afferent terminals, although actions at supraspinal sites may also occur and contribute to its clinical effect. Baclofen is a structural analog of the inhibitory neurotransmitter gamma-aminobutyric acid (GABA), and may exert its effects by stimulation of the GABA_B receptor subtype.

LIORESAL INTRATHECAL when introduced directly into the intrathecal space permits effective CSF concentrations to be achieved with resultant plasma concentrations 100 times less than those occurring with oral administration.

In people, as well as in animals, baclofen has been shown to have general CNS depressant properties as indicated by the production of sedation with tolerance, somnolence, ataxia, and respiratory and cardiovascular depression.

Pharmacodynamics of LIORESAL INTRATHECAL:

Intrathecal Bolus:

Adult Patients: The onset of action is generally one-half hour to one hour after an intrathecal bolus. Peak spasmolytic effect is seen at approximately four hours after dosing and effects may last four to eight hours. Onset, peak response, and duration of action may vary with individual patients depending on the dose and severity of symptoms.

Pediatric Patients: The onset, peak response and duration of action is similar to those seen in adult patients.

Continuous Infusion:

LIORESAL INTRATHECAL'S antispastic action is first seen at 6 to 8 hours after initiation of continuous infusion. Maximum activity is observed in 24 to 48 hours.

Continuous Infusion: No additional information is available for pediatric patients.

Pharmacokinetics of LIORESAL INTRATHECAL:

The pharmacokinetics of CSF clearance of LIORESAL INTRATHECAL calculated from intrathecal bolus or continuous infusion studies approximates CSF turnover, suggesting elimination is by bulk-flow removal of CSF.

Intrathecal Bolus: After a bolus lumbar injection of 50 or 100 mcg LIORESAL INTRATHECAL in seven patients, the average CSF elimination half-life was 1.51 hours over the first four hours and the average CSF clearance was approximately 30 ml/ hour.

Continuous Infusion: The mean CSF clearance for LIORESAL INTRATHECAL (baclofen injection) was approximately 30 ml/ hour in a study involving ten patients on continuous intrathecal infusion. Concurrent plasma concentrations of baclofen during intrathecal administration are expected to be low (0- 5 ng/ ml).

Limited pharmacokinetic data suggest that a lumbar-cisternal concentration gradient of about 4: 1 is established along the neuroaxis during baclofen infusion. This is based upon simultaneous CSF sampling via cisternal and lumbar tap in 5 patients receiving continuous baclofen infusion at the lumbar level at doses associated with therapeutic efficacy; the interpatient variability was great. The gradient was not altered by position.

Six pediatric patients (age 8- 18 years) receiving continuous intrathecal baclofen infusion at doses of 77- 400 mcg/ day had plasma baclofen levels near or below 10 ng/ ml.

INDICATIONS

LIORESAL INTRATHECAL is indicated for use in the management of severe spasticity. Patients should first respond to a screening dose of intrathecal baclofen prior to consideration for long term infusion via an implantable pump. For spasticity of spinal cord origin, chronic infusion of LIORESAL INTRATHECAL via an implantable pump 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 intrathecal baclofen therapy. LIORESAL INTRATHECAL (baclofen injection) is intended for use by the intrathecal route in single bolus test doses (via spinal catheter or lumbar puncture) and, for chronic use, only in implantable pumps approved by the FDA specifically for the administration of LIORESAL INTRATHECAL into the intrathecal space.

Spasticity of Spinal Cord Origin: Evidence supporting the efficacy of LIORESAL INTRATHECAL was obtained in randomized, controlled investigations that compared the effects of either a single intrathecal dose or a three day intrathecal infusion of LIORESAL INTRATHECAL to placebo in patients with severe spasticity and spasms due to either spinal cord trauma or multiple sclerosis. LIORESAL INTRATHECAL was superior to placebo on both principal outcome measures employed: change from baseline in the Ashworth rating of spasticity and the frequency of spasms.

Spasticity of Cerebral Origin: The efficacy of LIORESAL INTRATHECAL was investigated in three controlled clinical trials; two enrolled patients with cerebral palsy and one enrolled patients with spasticity due to previous brain injury. The first study, a randomized controlled cross-over trial of 51 patients with cerebral palsy, provided strong, statistically significant results; LIORESAL INTRATHECAL was superior to placebo in reducing spasticity as measured by the Ashworth Scale. A second cross-over study was conducted in 11 patients with spasticity arising from brain injury. Despite the small sample size, the study yielded a nearly significant test statistic (p= 0.066) and provided directionally favorable results. The last study, however, did not provide data that could be reliably analyzed.

LIORESAL INTRATHECAL therapy may be considered an alternative to destructive neurosurgical procedures. Prior to implantation of a device for chronic intrathecal infusion of LIORESAL INTRATHECAL, patients must show a response to LIORESAL INTRATHECAL in a screening trial (see Dosage and Administration).

CONTRAINDICATIONS

Hypersensitivity to baclofen. LIORESAL INTRATHECAL is not recommended for intravenous, intramuscular, subcutaneous or epidural administration.

WARNINGS

LIORESAL INTRATHECAL is for use in single bolus intrathecal injections (via a catheter placed in the lumbar intrathecal space or injection by lumbar puncture) and in implantable pumps approved by the FDA specifically for the intrathecal administration of baclofen. Because of the possibility of potentially life-threatening CNS depression, cardiovascular collapse, and/ or respiratory failure, physicians must be adequately trained and educated in chronic intrathecal infusion therapy.

The pump system should not be implanted until the patient's response to bolus LIORESAL INTRATHECAL injection is adequately evaluated. Evaluation (consisting of a screening procedure: see Dosage and Administration) requires that LIORESAL INTRATHECAL be administered into the intrathecal space via a catheter or lumbar puncture. Because of the risks associated with the screening procedure and the adjustment of dosage following pump implantation, these phases must be conducted in a medically supervised and adequately equipped environment following the instructions outlined in the Dosage and Administration section.

Resuscitative equipment should be available.

Following surgical implantation of the pump, particularly during the initial phases of pump use, the patient should be monitored closely until it is certain that the patient's response to the infusion is acceptable and reasonably stable.

On each occasion that the dosing rate of the pump and/ or the concentration of LIORESAL INTRATHECAL (baclofen injection) in the reservoir is adjusted, close medical monitoring is required until it is certain that the patient's response to the infusion is acceptable and reasonably stable.

It is mandatory that the patient, all patient caregivers, and the physicians responsible for the patient receive adequate information regarding the risks of this mode of treatment. All medical personnel and caregivers should be instructed in 1) the signs and symptoms of overdose, 2) procedures to be followed in the event of overdose and 3) proper home care of the pump and insertion site.

Overdose: Signs of overdose may appear suddenly or insidiously. Acute massive overdose may present as coma. Less sudden and/ or less severe forms of overdose may present with signs of drowsiness, lightheadedness, dizziness, somnolence, respiratory depression, seizures, rostral pro- gression of hypotonia and loss of consciousness progressing to coma. Should overdose appear likely, the patient should be taken immediately to a hospital for assessment and emptying of the pump reservoir. In cases reported to date, overdose has generally been related to pump malfunction or dosing error. (See Drug Overdose Symptoms and Treatment.)

Extreme caution must be used when filling an FDA approved implantable pump. Such pumps should only be refilled through the reservoir refill septum. However, some pumps are also equipped with a catheter access port that allows direct access to the intrathecal catheter. Direct injection into this catheter access port may cause a life-threatening overdose.

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.

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.

Fatalities:

Spasticity of Spinal Cord Origin: There were 16 deaths reported among the 576 U.S. patients treated with LIORESAL INTRATHECAL (baclofen injection) in pre- and post-marketing studies evaluated as of December 1992. Because these patients were treated under uncontrolled clinical settings, it is impossible to determine definitively what role, if any, LIORESAL INTRATHECAL played in their deaths. As a group, the patients who died were relatively young (mean age was 47 with a range from 25 to 63), but the majority suffered from severe spasticity of many years duration, were nonambulatory, had various medical complications such as pneumonia, urinary tract infections, and decubiti, and/or had received multiple concomitant medications. A case-by-case review of the clinical course of the 16 patients who died failed to reveal any unique signs, symptoms, or laboratory results that would suggest that treatment with LIORESAL INTRATHECAL caused their deaths. Two patients, however, did suffer sudden and unexpected death within 2 weeks of pump implantation and one patient died unexpectedly after screening.

One patient, a 44 year-old male with MS, died in hospital on the second day following pump implantation. An autopsy demonstrated severe fibrosis of the coronary conduction system. A second patient, a 52 year-old woman with MS and a history of an inferior wall myocardial infarction, was found dead in bed 12 days after pump implantation, 2 hours after having had documented normal vital signs. An autopsy revealed pulmonary congestion and bilateral pleural effusions. It is impossible to determine whether LIORESAL INTRATHECAL contributed to these deaths. The third patient underwent three baclofen screening trials. His medical history included SCI, aspiration pneumonia, septic shock, disseminated intravascular coagulopathy, severe metabolic acidosis, hepatic toxicity, and status epilepticus. Twelve days after screening (he was not implanted), he again experienced status epilepticus with subsequent significant neurological deterioration. Based upon prior instruction, extraordinary resuscitative measures were not pursued and the patient died.

Spasticity of Cerebral Origin: There were three deaths occurring among the 211 patients treated with LIORESAL INTRATHECAL in pre-marketing studies as of March 1996. These deaths were not attributed to the therapy.

PRECAUTIONS

Children should be of sufficient body mass to accommodate the implantable pump for chronic infusion. Please consult pump manufacturer's manual for specific recommendations.

Safety and effectiveness in pediatric patients below the age of 4 have not been established.

Screening

Patients should be infection-free prior to the screening trial with LIORESAL INTRATHECAL (baclofen injection) because the presence of a systemic infection may interfere with an assessment of the patient's response to bolus LIORESAL INTRATHECAL.

Pump Implantation

Patients should be infection-free prior to pump implantation because the presence of infection may increase the risk of surgical complications. Moreover, a systemic infection may complicate dosing.

Pump Dose Adjustment and Titration

In most patients, it will be necessary to increase the dose gradually over time to maintain effectiveness; a sudden requirement for substantial dose escalation typically indicates a catheter complication (i.e., catheter kink or dislodgement).

Reservoir refilling must be performed by fully trained and qualified personnel following the directions provided by the pump manufacturer. Refill intervals should be carefully calculated to prevent depletion of the reservoir, as this would result in the return of severe spasticity and possibly symptoms of withdrawal.

Strict aseptic technique in filling is required to avoid bacterial contamination and serious infection. A period of observation appropriate to the clinical situation should follow each refill or manipulation of the drug reservoir.

Extreme caution must be used when filling an FDA approved implantable pump equipped with an injection port that allows direct access to the intrathecal catheter. Direct injection into the catheter through the catheter access port may cause a life-threatening overdose.

Additional considerations pertaining to dosage adjustment: It may be important to titrate the dose to maintain some degree of muscle tone and allow occasional spasms to: 1) help support circulatory function, 2) possibly prevent the formation of deep vein thrombosis, 3) optimize activities of daily living and ease of care.

Except in overdose related emergencies, the dose of LIORESAL INTRATHECAL should ordinarily be reduced slowly if the drug is discontinued for any reason.

An attempt should be made to discontinue concomitant oral antispasticity medication to avoid possible overdose or adverse drug interactions, either prior to screening or following implant and initiation of chronic LIORESAL INTRATHECAL infusion. Reduction and discontinuation of oral anti-spasmodics should be done slowly and with careful monitoring by the physician. Abrupt reduction or discontinuation of concomitant antispastics should be avoided.

Drowsiness: Drowsiness has been reported in patients on LIORESAL INTRATHECAL. Patients should be cautioned regarding the operation of automobiles or other dangerous machinery, and activities made hazardous by decreased alertness. Patients should also be cautioned that the central nervous system depressant effects of LIORESAL INTRATHECAL (baclofen injection) may be additive to those of alcohol and other CNS depressants.

Precautions in special patient populations: Careful dose titration of LIORESAL INTRATHECAL is needed when spasticity is necessary to sustain upright posture and balance in locomotion or whenever spasticity is used to obtain optimal function and care.

Patients suffering from psychotic disorders, schizophrenia, or confusional states should be treated cautiously with LIORESAL INTRATHECAL and kept under careful surveillance, because exacerbations of these conditions have been observed with oral administration.

LIORESAL INTRATHECAL should be used with caution in patients with a history of autonomic dysreflexia. The presence of nociceptive stimuli or abrupt withdrawal of LIORESAL INTRATHECAL (baclofen injection) may cause an autonomic dysreflexic episode.

Because LIORESAL is primarily excreted unchanged by the kidneys, it should be given with caution in patients with impaired renal function and it may be necessary to reduce the dosage.

LABORATORY TESTS

No specific laboratory tests are deemed essential for the management of patients on LIORESAL INTRATHECAL.

DRUG INTERACTIONS

There is inadequate systematic experience with the use of LIORESAL INTRATHECAL in combination with other medications to predict specific drug-drug interactions. Interactions attributed to the combined use of LIORESAL INTRATHECAL and epidural morphine include hypotension and dyspnea.

CARCINOGENESIS, MUTAGENESIS, AND IMPAIRMENT OF FERTILITY

No increase in tumors was seen in rats receiving LIORESAL (baclofen USP) orally for two years at approximately 30-60 times on a mg/kg basis, or 10-20 times on a mg/m² basis, the maximum oral dose recommended for human use. Mutagenicity assays with LIORESAL have not been performed.

PREGNANCY CATEGORY C

LIORESAL (baclofen USP) given orally has been shown to increase the incidence of omphaloceles (ventral hernias) in fetuses of rats given approximately 13 times on a mg/kg basis, or 3 times on a mg/m² basis, the maximum oral dose recommended for human use; this dose also caused reductions in food intake and weight gain in the dams.

This abnormality was not seen in mice or rabbits. There are no adequate and well-controlled studies in pregnant women. LIORESAL should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

NURSING MOTHERS

In mothers treated with oral LIORESAL (baclofen USP) in therapeutic doses, the active substance passes into the breast milk. It is not known whether detectable levels of drug are present in breast milk of nursing mothers receiving LIORESAL INTRATHECAL. As a general rule, nursing should be undertaken while a patient is receiving LIORESAL INTRATHECAL only if the potential benefit justifies the potential risks to the infant.

PEDIATRIC USE

Children should be of sufficient body mass to accommodate the implantable pump for chronic infusion. Please consult pump manufacturer's manual for specific recommendations.

Safety and effectiveness in pediatric patients below the age of 4 have not been established.

Considerations based on experience with oral LIORESAL (baclofen USP)

A dose-related increase in incidence of ovarian cysts was observed in female rats treated chronically with oral LIORESAL. Ovarian cysts have been found by palpation in about 4% of the multiple sclerosis patients who were treated with oral LIORESAL for up to one year. In most cases these cysts disappeared spontaneously while patients continued to receive the drug. Ovarian cysts are estimated to occur spontaneously in approximately 1% to 5% of the normal female population.

ADVERSE DRUG EVENTS

Spasticity of Spinal Cord Origin:

Commonly Observed in Patients with Spasticity of Spinal Origin — In pre- and post-marketing clinical trials, the most commonly observed adverse events associated with use of LIORESAL INTRATHECAL (baclofen injection) which were not seen at an equivalent incidence among placebo-treated patients were: somnolence, dizziness, nausea, hypotension, headache, convulsions and hypotonia.

Associated with Discontinuation of Treatment — 8/474 patients with spasticity of spinal cord origin receiving long term infusion of LIORESAL INTRATHECAL in pre- and post-marketing clinical studies in the U.S. discontinued treatment due to adverse events. These include: pump pocket infections (3), meningitis (2), wound dehiscence (1), gynecological fibroids (1) and pump overpressurization (1) with unknown, if any, sequela. Eleven patients who developed coma secondary to overdose had their treatment temporarily suspended, but all were subsequently re-started and were not, therefore, considered to be true discontinuations.

Fatalities — See Warnings.

Incidence in Controlled Trials — Experience with LIORESAL INTRATHECAL (baclofen injection) obtained in parallel, placebo-controlled, randomized studies provides only a limited basis for estimating the incidence of adverse events because the studies were of very brief duration (up to three days of infusion) and involved only a total of 63 patients. The following events occurred among the 31 patients receiving LIORESAL INTRATHECAL (baclofen injection) in two randomized, placebo-controlled trials: hypotension (2), dizziness (2), headache (2), dyspnea (1). No adverse events were reported among the 32 patients receiving placebo in these studies.

Events Observed during the Pre- and Post-marketing Evaluation of LIORESAL INTRATHECAL — Adverse events associated with the use of LIORESAL INTRATHECAL reflect experience gained with 576 patients followed prospectively in the United States. They received LIORESAL INTRATHECAL for periods of one day (screening) (N = 576) to over eight years (maintenance) (N = 10). The usual screening bolus dose administered prior to pump implantation in these studies was typically 50 mcg. The maintenance dose ranged from 12 mcg to 2003 mcg per day. Because of the open, uncontrolled nature of the experience, a causal linkage between events observed and the administration of LIORESAL INTRATHECAL cannot be reliably assessed in many cases and many of the adverse events reported are known to occur in association with the underlying conditions being treated. Nonetheless, many of the more commonly reported reactions—hypotonia, somnolence, dizziness, paresthesia, nausea/vomiting and headache—appear clearly drug-related.

Adverse experiences reported during all U.S. studies (both controlled and uncontrolled) are shown in the following table. Eight of 474 patients who received chronic infusion via implanted pumps had adverse experiences which led to a discontinuation of long term treatment in the pre- and post-marketing studies.

INCIDENCE OF MOST FREQUENT (≥1%) ADVERSE EVENTS IN PATIENTS WITH SPASTICITY OF SPINAL ORIGIN IN PROSPECTIVELY MONITORED CLINICAL TRIALS

Adverse Event	Percent of Patients Reporting Events		
	N = 576	N = 474	N = 430
	Screening ^a Percent	Titration ^b Percent	Maintenance ^c Percent
Hypotonia	5.4	13.5	25.3
Somnolence	5.7	5.9	20.9
Dizziness	1.7	1.9	7.9
Paresthesia	2.4	2.1	6.7
Nausea and Vomiting	1.6	2.3	5.6
Headache	1.6	2.5	5.1
Constipation	0.2	1.5	5.1
Convulsion	0.5	1.3	4.7
Urinary Retention	0.7	1.7	1.9
Dry Mouth	0.2	0.4	3.3
Accidental Injury	0.0	0.2	3.5
Asthenia	0.7	1.3	1.4
Confusion	0.5	0.6	2.3
Death	0.2	0.4	3.0
Pain	0.0	0.6	3.0
Speech Disorder	0.0	0.2	3.5
Hypotension	1.0	0.2	1.9
Ambyopia	0.5	0.2	2.3
Diarrhea	0.0	0.8	2.3
Hypoventilation	0.2	0.8	2.1
Coma	0.0	1.5	0.9
Impotence	0.2	0.4	1.6
Peripheral Edema	0.0	0.0	2.3
Urinary Incontinence	0.0	0.8	1.4
Insomnia	0.0	0.4	1.6
Anxiety	0.2	0.4	0.9
Depression	0.0	0.0	1.6
Dyspnea	0.3	0.0	1.2
Fever	0.5	0.2	0.7
Pneumonia	0.2	0.2	1.2
Urinary Frequency	0.0	0.6	0.9
Urticaria	0.2	0.2	1.2
Anorexia	0.0	0.4	0.9
Diplopia	0.0	0.4	0.9
Dysautonomia	0.2	0.2	0.9
Hallucinations	0.3	0.4	0.5
Hypertension	0.2	0.6	0.5

^a Following administration of test bolus

^b Two month period following implant

^c Beyond two months following implant

N= total number of patients entering each period

%=% of patients evaluated

In addition to the more common (1% or more) adverse events reported in the prospectively followed 576 domestic patients in pre- and post- marketing studies, experience from an additional 194 patients exposed to LIORESAL INTRATHECAL (baclofen injection) from foreign studies has been reported. The following adverse events, not described in the table, and arranged in decreasing order of frequency, and classified by body system, were reported:

Nervous System: Abnormal gait, thinking abnormal, tremor, amnesia, twitching, vasodilatation, cerebrovascular accident, nystagmus, personality disorder, psychotic depression, cerebral ischemia, emotional lability, euphoria, hypertonia, ileus, drug dependence, incoordination, paranoid reaction and ptosis.

Digestive System: Flatulence, dysphagia, dyspepsia and gastroenteritis.

Cardiovascular: Postural hypotension, bradycardia, palpitations, syncope, arrhythmia ventricular, deep thrombophlebitis, pallor and tachycardia.

Respiratory: Respiratory disorder, aspiration pneumonia, hyperventilation, pulmonary embolus and rhinitis.

Urogenital: Hematuria and kidney failure.

Skin and Appendages: Alopecia and sweating.

Metabolic and Nutritional Disorders: Weight loss, albuminuria, dehydration and hyperglycemia.

Special Senses: Abnormal vision, abnormality of accommodation, photophobia, taste loss and tinnitus.

Body as a Whole: Suicide, lack of drug effect, abdominal pain, hypothermia, neck rigidity, chest pain, chills, face edema, flu syndrome and overdose.

Hemic and Lymphatic System: Anemia.

Spasticity of Cerebral Origin:

Commonly Observed — In pre- marketing clinical trials, the most commonly observed adverse events associated with use of LIORESAL INTRATHECAL (baclofen injection) which were not seen at an equivalent incidence among placebo-treated patients included: agitation, constipation, somnolence, leukocytosis, chills, urinary retention and hypotonia.

Associated with Discontinuation of Treatment — Nine of 211 patients receiving LIORESAL INTRATHECAL in pre-marketing clinical studies in the U.S. discontinued long term infusion due to adverse events associated with intrathecal therapy.

The nine adverse events leading to discontinuation were: infection (3), CSF leaks (2), meningitis (2), drainage (1), and unmanageable trunk control (1).

Fatalities — Three deaths, none of which were attributed to LIORESAL INTRATHECAL, were reported in patients in clinical trials involving patients with spasticity of cerebral origin. See Warnings on other deaths reported in spinal spasticity patients.

Incidence in Controlled Trials — Experience with LIORESAL INTRATHECAL (baclofen injection) obtained in parallel, placebo-controlled, randomized studies provides only a limited basis for estimating the incidence of adverse events because the studies involved a total of 62 patients exposed to a single 50 mcg intrathecal bolus. The following events occurred among the 62 patients receiving LIORESAL INTRATHECAL in two randomized, placebo-controlled trials involving cerebral palsy and head injury patients, respectively: agitation, constipation, somnolence, leukocytosis, nausea, vomiting, nystagmus, chills, urinary retention, and hypotonia.

Events Observed during the Pre-marketing Evaluation of LIORESAL INTRATHECAL — Adverse events associated with the use of LIORESAL INTRATHECAL reflect experience gained with a total of 211 U. S. patients with spasticity of cerebral origin, of whom 112 were pediatric patients (under age 16 at enrollment). They received LIORESAL INTRATHECAL for periods of one day (screening) (N= 211) to 84 months (maintenance) (N= 1). The usual screening bolus dose administered prior to pump implantation in these studies was 50- 75 mcg. The maintenance dose ranged from 22 mcg to 1400 mcg per day. Doses used in this patient population for long term infusion are generally lower than those required for patients with spasticity of spinal cord origin.

Because of the open, uncontrolled nature of the experience, a causal linkage between events observed and the administration of LIORESAL INTRATHECAL cannot be reliably assessed in many cases. Nonetheless, many of the more commonly reported reactions— somnolence, dizziness, headache, nausea, hypotension, hypotonia and coma— appear clearly drug-related.

The most frequent (≥1%) adverse events reported during all clinical trials are shown in the following table. Nine patients discontinued long term treatment due to adverse events.

INCIDENCE OF MOST FREQUENT (≥ 1%) ADVERSE EVENTS IN PATIENTS WITH SPASTICITY OF CEREBRAL ORIGIN IN PROSPECTIVELY MONITORED CLINICAL TRIALS

Adverse Event	Percent of Patients Reporting Events		
	N = 211	N = 153	N = 150
	Screening ^a	Titration ^b	Maintenance ^c
	Percent	Percent	Percent
Hypotonia	2.4	14.4	34.7
Somnolence	7.6	10.5	18.7
Headache	6.6	7.8	10.7
Nausea and Vomiting	6.6	10.5	4.0
Vomiting	6.2	8.5	4.0
Urinary Retention	0.9	6.5	8.0
Convulsion	0.9	3.3	10.0
Dizziness	2.4	2.6	8.0
Nausea	1.4	3.3	7.3
Hypoventilation	1.4	1.3	4.0
Hypertonia	0.0	0.7	6.0
Paresthesia	1.9	0.7	3.3
Hypotension	1.9	0.7	2.0
Increased Salivation	0.0	2.6	2.7
Back Pain	0.9	0.7	2.0
Constipation	0.5	1.3	2.0
Pain	0.0	0.0	4.0
Pruritus	0.0	0.0	4.0
Diarrhea	0.5	0.7	2.0
Peripheral Edema	0.0	0.0	3.3
Thinking Abnormal	0.5	1.3	0.7
Agitation	0.5	0.0	1.3
Asthenia	0.0	0.0	2.0
Chills	0.5	0.0	1.3
Coma	0.5	0.0	1.3
Dry Mouth	0.5	0.0	1.3
Pneumonia	0.0	0.0	2.0
Speech Disorder	0.5	0.7	0.7
Tremor	0.5	0.0	1.3
Urinary Incontinence	0.0	0.0	2.0
Urination Impaired	0.0	0.0	2.0

^a Following administration of test bolus

^b Two month period following implant

^c Beyond two months following implant

N= Total number of patients entering each period. 211 patients received drug; (1 of 212) received placebo only.

The more common (1% or more) adverse events reported in the prospectively followed 211 patients exposed to LIORESAL INTRATHECAL (baclofen injection) have been reported. In the total cohort, the following adverse events, not described in the table, and arranged in decreasing order of frequency, and classified by body system, were reported:

Nervous System: Akathisia, ataxia, confusion, depression, opisthotonos, amnesia, anxiety, hallucinations, hysteria, insomnia, nystagmus, personality disorder, reflexes decreased, and vasodilatation.

Digestive System: Dysphagia, fecal incontinence, gastrointestinal hemorrhage and tongue disorder.

Cardiovascular: Bradycardia.

Respiratory: Apnea, dyspnea and hyperventilation.

Urogenital: Abnormal ejaculation, kidney calculus, oliguria and vaginitis.

Skin and Appendages: Rash, sweating, alopecia, contact dermatitis and skin ulcer.

Special Senses: Abnormality of accommodation.

Body as a Whole: Death, fever, abdominal pain, carcinoma, malaise and hypothermia.

Hemic and Lymphatic System: Leukocytosis and petechial rash.

DRUG OVERDOSE

Special attention must be given to recognizing the signs and symptoms of overdosage, especially during the initial screening and dose- titration phase of treatment, but also during reintroduction of LIORESAL INTRATHECAL after a period of interruption in therapy.

Symptoms of LIORESAL INTRATHECAL Overdose: Drowsiness, lightheadedness, dizziness, somnolence, respiratory depression, seizures, rostral progression of hypotonia and loss of consciousness progressing to coma of up to 72 hr. duration. In most cases reported, coma was reversible without sequelae after drug was discontinued. Symptoms of LIORESAL INTRATHECAL overdose were reported in a sensitive adult patient after receiving a 25 mcg intrathecal bolus.

Treatment Suggestions for Overdose:

There is no specific antidote for treating overdoses of LIORESAL INTRATHECAL (baclofen injection); however, the following steps should ordinarily be undertaken:

- 1) Residual LIORESAL INTRATHECAL solution should be removed from the pump as soon as possible.
- 2) Patients with respiratory depression should be intubated if necessary, until the drug is eliminated.

Anecdotal reports suggest that intravenous physostigmine may reverse central side effects, notably drowsiness and respiratory depression. Caution in administering physostigmine is advised, however, because its use has been associated with the induction of seizures and bradycardia.

Physostigmine Doses for Adult Patients: Administer 2 mg of physostigmine intramuscularly or intravenously at a slow controlled rate of no more than 1 mg per minute. Dosage may be repeated if life- threatening signs, such as arrhythmia, convulsions or coma occur.

Physostigmine Doses for Pediatric Patients: Administer 0.02 mg/ kg physostigmine intramuscularly or intravenously, do not give more than 0.5 mg per minute. The dosage may be repeated at 5 to 10 minute intervals until a therapeutic effect is obtained or a maximum dose of 2 mg is attained.

Physostigmine may not be effective in reversing large overdoses and patients may need to be maintained with respiratory support.

If lumbar puncture is not contraindicated, consideration should be given to withdrawing 30- 40 ml of CSF to reduce CSF baclofen concentration.

DOSAGE AND ADMINISTRATION

Refer to the manufacturer’s manual for the implantable pump approved for intrathecal infusion for specific instructions and precautions for programming the pump and/ or refilling the reservoir. There are various pumps with varying reservoir volumes and there are various refill kits available. It is important to be familiar with all of these products in order to select the appropriate refill kit for the particular pump in use.

Screening Phase: Prior to pump implantation and initiation of chronic infusion of LIORESAL INTRATHECAL (baclofen injection), patients must demonstrate a positive clinical response to a LIORESAL INTRATHECAL bolus dose administered intrathecally in a screening trial. The screening trial employs LIORESAL INTRATHECAL at a concentration of 50 mcg/ ml. A 1 ml ampule (50 mcg/ ml) is available for use in the screening trial. The screening procedure is as follows. An initial bolus containing 50 micrograms in a volume of 1 milliliter is administered into the intrathecal space by barbotage over a period of not less than one minute. The patient is observed over the ensuing 4 to 8 hours. A positive response consists of a significant decrease in muscle tone and/ or frequency and/ or severity of spasms. If the initial response is less than desired, a second bolus injection may be administered 24 hours after the first. The second screening bolus dose consists of 75 micrograms in 1.5 milliliters. Again, the patient should be observed for an interval of 4 to 8 hours. If the response is still inadequate, a final bolus screening dose of 100 micrograms in 2 milliliters may be administered 24 hours later.

Pediatric Patients: The starting screening dose for pediatric patients is the same as in adult patients, i.e., 50 mcg. However, for very small patients, a screening dose of 25 mcg may be tried first. **Patients who do not respond to a 100 mcg intrathecal bolus should not be considered candidates for an implanted pump for chronic infusion.**

Post- Implant Dose Titration Period: To determine the initial total daily dose of LIORESAL INTRATHECAL following implant, the screening dose that gave a positive effect should be doubled and administered over a 24- hour period, unless the efficacy of the bolus dose was maintained for more than 8 hours, in which case the starting daily dose should be the screening dose delivered over a 24-hour period. No dose increases should be given in the first 24 hours (i.e., until the steady state is achieved).

Adult Patients with Spasticity of Spinal Cord Origin: After the first 24 hours, for adult patients, the daily dosage should be increased slowly by 10- 30% increments and only once every 24 hours, until the desired clinical effect is achieved.

Adult Patients with Spasticity of Cerebral Origin: After the first 24 hours, the daily dose should be increased slowly by 5- 15% only once every 24 hours, until the desired clinical effect is achieved.

Pediatric Patients: After the first 24 hours, the daily dose should be increased slowly by 5-15% only once every 24 hours, until the desired clinical effect is achieved. If there is not a substantive clinical response to increases in the daily dose, check for proper pump function and catheter patency. Patients must be monitored closely in a fully equipped and staffed environment during the screening phase and dose- titration period immediately following implant. Resuscitative equipment should be immediately available for use in case of life- threatening or intolerable side effects.

Maintenance Therapy:

Spasticity of Spinal Cord Origin Patients: The clinical goal is to maintain muscle tone as close to normal as possible, and to minimize the frequency and severity of spasms to the extent possible, without inducing intolerable side effects. Very often, the maintenance dose needs to be adjusted during the first few months of therapy while patients adjust to changes in life style due to the alleviation of spasticity. During periodic refills of the pump, the daily dose may be increased by 10-40%, but no more than 40%, to maintain adequate symptom control. The daily dose may be reduced by 10-20% if patients experience side effects. Most patients require gradual increases in dose over time to maintain optimal response during chronic therapy. A sudden large requirement for dose escalation suggests a catheter complication (i.e., catheter kink or dislodgement).

Maintenance dosage for long term continuous infusion of LIORESAL INTRATHECAL (baclofen injection) has ranged from 12 mcg/ day to 2003 mcg/ day, with most patients adequately maintained on 300 micrograms to 800 micrograms per day. There is limited experience with daily doses greater than 1000 mcg/ day. Determination of the optimal LIORESAL INTRATHECAL dose requires individual titration. The lowest dose with an optimal response should be used.

Spasticity of Cerebral Origin Patients: The clinical goal is to maintain muscle tone as close to normal as possible and to minimize the frequency and severity of spasms to the extent possible, without inducing intolerable side effects, or to titrate the dose to the desired degree of muscle tone for optimal functions. Very often the maintenance dose needs to be adjusted during the first few months of therapy while patients adjust to changes in life style due to the alleviation of spasticity. During periodic refills of the pump, the daily dose may be increased by 5 - 20%, but no more than 20%, to maintain adequate symptom control. The daily dose may be reduced by 10-20% if patients experience side effects. Many patients require gradual increases in dose over time to maintain optimal response during chronic therapy. A sudden large requirement for dose escalation suggests a catheter complication (i.e., catheter kink or dislodgement).

Maintenance dosage for long term continuous infusion of LIORESAL INTRATHECAL (baclofen injection) has ranged from 22 mcg/ day to 1400 mcg/ day, with most patients adequately maintained on 90 micrograms to 703 micrograms per day. In clinical trials, only 3 of 150 patients required daily doses greater than 1000 mcg/ day.

Pediatric Patients: Use same dosing recommendations for patients with spasticity of cerebral origin. Pediatric patients under 12 years seemed to require a lower daily dose in clinical trials. Average daily dose for patients under 12 years was 274 mcg/ day, with a range of 24 to 1199 mcg/ day. Dosage requirement for pediatric patients over 12 years does not seem to be different from that of adult patients. Determination of the optimal LIORESAL INTRATHECAL dose requires individual titration. The lowest dose with an optimal response should be used.

Potential need for dose adjustments in chronic use: During long term treatment, approximately 5% (28/627) of patients become refractory to increasing doses. There is not sufficient experience to make firm recommendations for tolerance treatment; however, this "tolerance" has been treated on occasion, in hospital, by a "drug holiday" consisting of the gradual reduction of LIORESAL INTRATHECAL over a 2 to 4 week period and switching to alternative methods of spasticity management. After the "drug holiday," LIORESAL INTRATHECAL may be restarted at the initial continuous infusion dose.

Stability

Parenteral drug products should be inspected for particulate matter and discoloration prior to administration, whenever solution and container permit.

Delivery Specifications

The specific concentration that should be used depends upon the total daily dose required as well as the delivery rate of the pump. LIORESAL INTRATHECAL may require dilution when used with certain implantable pumps. Please consult manufacturer's manual for specific recommendations.

Preparation Instruction:

Screening

Use the 1 ml screening ampule only (50 mcg/ml) for bolus injection into the subarachnoid space. For a 50mcg bolus dose, use 1 ml of the screening ampule. Use 1.5 ml of 50 mcg/ml baclofen injection for a 75 mcg bolus dose. For the maximum screening dose of 100 mcg, use 2 ml of 50 mcg/ml baclofen injection (2 screening ampules).

Maintenance

For patients who require concentrations other than 500 mcg/ml or 2000 mcg/ml, LIORESAL INTRATHECAL **must be diluted**.

LIORESAL INTRATHECAL **must be diluted** with sterile preservative free Sodium Chloride for Injection, U.S.P.

Delivery Regimen:

LIORESAL INTRATHECAL is most often administered in a continuous infusion mode immediately following implant. For those patients implanted with programmable pumps who have achieved relatively satisfactory control on continuous infusion, further benefit may be attained using more complex schedules of LIORESAL INTRATHECAL delivery. For example, patients who have increased spasms at night may require a 20% increase in their hourly infusion rate. Changes in flow rate should be programmed to start two hours before the time of desired clinical effect.

HOW SUPPLIED

LIORESAL INTRATHECAL (baclofen injection) is available in single use ampules of 10 mg/20 ml (500 mcg/ ml) or 10 mg/ 5 ml (2000 mcg/ml) or 40 mg/20 ml (2000 mcg/ml) packaged in a Refill Kit for intrathecal administration. For screening, LIORESAL INTRATHECAL is available in a single use ampule of 0.05 mg/ 1 ml.

Model 8561 LIORESAL INTRATHECAL Refill Kit contains one ampule of 10 mg/ 20 ml (500 mcg/ml) (NDC 58281-560-01).

Model 8562 LIORESAL INTRATHECAL Refill Kit contains two ampules of 10 mg/ 5 ml (2000 mcg/ml) (NDC 58281-561-02).

Model 8563 LIORESAL INTRATHECAL contains one ampule of 0.05 mg/ 1 ml (NDC 58281-562-01).

Model 8564 LIORESAL INTRATHECAL Refill Kit contains four ampules of 10 mg/ 5 ml (2000 mcg/ml) (NDC 58281-561-04) or one ampule of 40 mg/20 ml (2000 mcg/ml) (NDC 58281-563-01).

Model 8565 LIORESAL INTRATHECAL Refill Kit contains two ampules of 10 mg/ 20 ml (500 mcg/ml) (NDC 58281-560-02).

Model 8566 LIORESAL INTRATHECAL Refill Kit contains eight ampules of 10 mg/ 5 ml (2000 mcg/ml) (NDC 58281-561-08) or two ampules of 40 mg/20 ml (2000 mcg/ml) (NDC 58281-563-02).

STORAGE

- Does not require refrigeration.
- Do not store above 86° F (30° C).
- Do not freeze.
- Do not heat sterilize.

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