Dear Health Care Professional,

This letter is to inform you of a potential pump motor stall issue that affects SynchroMed EL pumps with motors manufactured prior to September 1999. This population of pumps can stall at a higher rate due to gear shaft wear. If a pump motor stall occurs, drug delivery will stop abruptly and without warning resulting in loss of therapy, return of underlying symptoms, and/or symptoms of drug underinfusion or withdrawal. Drug withdrawal from Intrathecal Baclofen (ITB) therapy can be fatal if not treated promptly and effectively.1,2

**Affected Devices**

Medtronic estimates that approximately 8,000 pumps from this population remain implanted worldwide. Because this failure mode is random, it is not possible to predict which of these devices may fail in the future. The enclosed list of pump serial numbers and patient names identifies your patients who, according to our device registration records, are currently implanted with pumps in this affected population.

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1 For information on baclofen withdrawal refer to the Lioresal® Intrathecal (baclofen injection) Package Insert, Copyright Medtronic Inc. 2002 www.medtronic.com/lioresaipi

Urgent: Medical Device Correction
Pumps with Motors Manufactured Prior to September 1999

As of June 15, 2007, Medtronic has received 354 health care professional inquiries/complaints worldwide which have been confirmed, through returned product analysis, to be due to gear shaft wear. Medtronic has determined that 220 of these events are associated with the subset of devices that are the subject of this letter. Medtronic has submitted Medical Device Reporting (MDR’s) to the FDA for all 354 cases. No patient deaths or permanent injuries have been directly attributed to pump motor stall due to gear shaft wear. The following table provides an overview of these MDR’s.

<table>
<thead>
<tr>
<th>MDR Overview</th>
<th>MDR Qty</th>
<th>% Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Return of underlying symptoms</td>
<td>94</td>
<td>43%</td>
</tr>
<tr>
<td>No Symptoms Reported*</td>
<td>86</td>
<td>39%</td>
</tr>
<tr>
<td>Withdrawal</td>
<td>34</td>
<td>15%</td>
</tr>
<tr>
<td>Overdose</td>
<td>4</td>
<td>2%</td>
</tr>
<tr>
<td>Death (not associated with motor stall)</td>
<td>2</td>
<td>1%</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>220</strong></td>
<td><strong>100%</strong></td>
</tr>
</tbody>
</table>

(*No symptoms reported: end of service, malfunction, volume discrepancy, return w/o complaint)

The highest reported rate of pump motor stalls due to gear shaft wear has been among patients who are administered ITB therapy. Using Medtronic’s Returned Product Analysis data, this subset of pumps exhibits a cumulative gear shaft wear failure rate of 2.2%, at 7 years post implant. SynchroMed EL pumps have an expected battery longevity between 78 and 90 months (between 6.6 to 7.5 years), depending on daily infusion rate. This means that most of the affected pumps in this subset of devices are either at or approaching normal end of battery life. Physicians should consider this battery life information when discussing treatment options with their patients. Please refer to the enclosed Figures 1 and 2 for details regarding ITB and Pain failure rates.

This specific gear shaft wear issue does not affect the SynchroMed II pump, because the SynchroMed II pump has a different motor design.

Patient Risk

Pump motor stalls due to gear shaft wear result in the abrupt cessation of therapy. After a patient presents with symptoms of underinfusion, a clinician can only confirm a pump motor stall condition via drug refill volume discrepancy and x-ray pump roller study (refer to the attached Pump Stall Troubleshooting Procedure).

The SynchroMed EL pump does not provide an alarm to alert the patient or clinician to a stalled motor condition.

The affected patient population can experience the following signs and symptoms:

---

3 Based on analysis of available data, there is no evidence that the type of drugs used in the different patient populations can account for the difference observed in gear shaft wear failure rates. Spasticity patients exhibit more clinically obvious signs of therapy cessation which may be responsible for an increased rate of pump motor stall detection and reporting.

4 Medtronic ITB Clinical Reference Guide; UC199601184b EN NP2584b
• Abrupt cessation of ITB therapy which can lead to serious medical complications and, if not treated promptly and effectively, can be fatal. Also, ITB patients have a higher risk of serious medical complications that are potentially life threatening, if their device fails, than pump patients receiving other Medtronic approved infusion therapies.

• Abrupt cessation of morphine for intrathecal pain therapy, which can result in a return of underlying symptoms and/or withdrawal symptoms.

• Abrupt cessation of chemotherapy for hepatic arterial infusion, which can result in missing part or all of the planned treatment. This can have potentially serious consequences for the patient.

• To ascertain the patient risk associated with abrupt cessation of other drugs being administered via the pump, refer to the applicable drug labeling and/or the most current Physician’s Desk Reference5.

Because this failure mode is random, it is not possible to predict which of these devices may fail in the future.

Patient Management Recommendations

We realize that each of your patients is unique, and we support your clinical judgment in caring for them. Sample patient letters for intrathecal baclofen (ITB) therapy and pain therapy patients are attached for your convenience, should you choose to use them. If you are concerned about motor stalls in implanted devices, please consider Medtronic’s patient management recommendations below.

Patient Management Recommendation #1

If a patient presents symptoms of underinfusion or withdrawal, a clinician can confirm a pump motor stall through a drug refill volume discrepancy and x-ray pump roller study (refer to the attached Pump Stall Troubleshooting Procedure6). If a pump motor stall is confirmed, immediate replacement of this pump is necessary for continued intrathecal therapy.

Patient Management Recommendation #2

Discuss this important information with your patients and caregivers, reminding them that pumps can fail without warning, and that the patient may not become aware of the pump failure until he/she experiences return of underlying symptoms, and/or symptoms of drug withdrawal.

Patient Management Recommendation #3

Educate patients and caregivers about the early signs and symptoms of drug underdose or withdrawal.

Patient Management Recommendation #4

Instruct patients to seek immediate medical assistance in the event that signs or symptoms of drug underdose or withdrawal appear.

5 Note that the SynchroMed EL pump is approved for use with Lioresal and morphine.
6 Medtronic ITB Clinical Reference Guide; UC199601184b EN NP2584b
Recommendations for Specific Therapies
In addition, please consider the following information for the appropriate therapy segment:

- **ITB Therapy:** Use your professional medical judgment in considering early pump replacement due to the potentially severe medical consequences of ITB withdrawal. You and your patients should be vigilant for early symptoms of ITB withdrawal. These may include a return of baseline spasticity, pruritis, hypotention, parasthesias, high fever, and/or altered mental status. 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 baclofen or ITB). **Please refer to the enclosed “Lioresal® Intrathecal (Baclofen Injection) Emergency Procedures Sheet” and “Lioresal Emergency Medication Information Patient Wallet Card” for patient management recommendations.** (Additional copies of each of these publications are available free of charge from your Medtronic representative.)

- **Intrathecal Pain Therapy:** Determine whether early pump replacement is medically appropriate, considering the risks incident to continued pump usage as compared to risks incident to a pump replacement procedure. As always, you and your patients should be vigilant for early symptoms of drug underdose or withdrawal.

- **Chemotherapy:** Determine whether early pump replacement or other type of medical treatment is appropriate, considering the risks incident to continued pump usage as compared to risks incident to a pump replacement procedure.

Next Steps

1. FDA has knowledge of this SynchroMed® EL Gear Shaft Wear recall communication. **Your local Medtronic representative will follow up with you to review this information and confirm notification.**

2. Report any malfunction or adverse event related to this device to Medtronic Neuromodulation Technical Services at 1-800-707-0933, and to the FDA’s MedWatch Program by phone at 1-800-FDA-1088, by Fax at 1-800-FDA-0178, by mail at MedWatch, HF-2, FDA, 5600 Fishers Lane, Rockville, MD 20852-9787, or on the MedWatch website at [www.fda.gov/medwatch](http://www.fda.gov/medwatch).

3. **Should you decide to replace any pumps in this population, please return the explanted SynchroMed EL pumps to Medtronic Returned Products Analysis. Please contact Medtronic Neuromodulation Technical Services at 1-800-707-0933, or your local Medtronic representative to facilitate the device return procedure, if you need assistance.**

Physician and Patient Support

We appreciate your assistance with this matter. To address the impact of any inconvenience that patients experience related to early replacement surgery, Medtronic will reimburse patients up to $1,000 of reasonable, non-reimbursed expenses incurred in connection with surgical procedures taken to explant the device, in accordance with Medtronic’s applicable Supplemental Limited Warranty. The sample patient letters enclosed provides further information about how patients should seek such reimbursement.

The following resources are available for additional assistance.

- Patients may contact Medtronic Neuromodulation Patient Services at 1-800-510-6735.
- Physicians may contact Medtronic Neuromodulation Technical Services at 1-800-707-0933 or their local Medtronic representative.

We appreciate your assistance with this matter. We regret and apologize for the inconvenience this matter may have caused you and your patients. We are committed to providing you with the highest quality products, services and ongoing support as you care for your patients.

For immediate assistance, please contact your local Medtronic representative.

Sincerely,

George Aram
VP Quality
Medtronic Neuromodulation Sector

Enclosures:

- Patient/Pump Serial Number List
- Figure 1: “SynchroMed EL Survival Plot – ITB Therapy”
- Figure 2: “SynchroMed EL Survival Plot – Pain Therapy”
- Pump Stall Troubleshooting Procedure
- Lioresal® Intrathecal (Baclofen Injection) Emergency Procedures Sheet
- Lioresal Emergency Medication Information Patient Wallet Card
- Sample Patient Letters
Figure 1 provides cumulative survival curves for the gear shaft wear failure mode with 95% confidence bounds for two pump populations (those that contain motors manufactured prior to September 1999 vs. those containing motors manufactured beginning September 1999 and beyond).

The cumulative survival estimate for motors manufactured prior to September 1999 is 97.8% at 7 years (84 months) post implant. This equates to a cumulative failure rate of 2.2% at 7 years.

The cumulative survival estimate for motors manufactured beginning September 1999 and beyond is 99.5% at 7 years (84 months) post implant. This equates to a cumulative failure rate of 0.5% at 7 years.
Figure 2 provides cumulative survival curves for the gear shaft wear failure mode for pain patients with 95% confidence bounds for two pump populations (those that contain motors manufactured prior to September 1999 vs. those containing motors manufactured beginning September 1999 and beyond).

The cumulative survival estimate for motors manufactured prior to September 1999 is 98.7% at 7 years (84 months) post implant. This equates to a cumulative failure rate of 1.3% at 7 years.

The cumulative survival estimate for motors manufactured beginning September 1999 and beyond is 99.7% at 7 years (84 months) post implant. This equates to a cumulative failure rate of 0.3% at 7 years.
Dear [Patient Name]:

Medtronic, Inc., the manufacturer of your implantable pump, has recently informed us of a pump reliability concern. The motor component within your pump may stall and could result in decreased amount of the drug being delivered or not being delivered at all through the catheter. Although the chance of this happening to your pump is rather low, *if it occurs, it could cause drug delivery to stop abruptly, resulting in loss of therapy, return of your underlying symptoms, and symptoms of drug underinfusion or withdrawal.*

As you may know, the pump that delivers your therapy has an average battery life of 5 to 7 years. Because your pump is nearing its normal end of battery life, you may wish to consider having the pump replaced now. Please contact our office at XXX-XXX-XXXX, to discuss your options. As always, if you have any question or concerns, please contact our office.

To address the impact of any inconvenience that you may experience related to early replacement surgery, Medtronic will reimburse you up to $1,000 of reasonable, non-reimbursed expenses incurred in connection with surgical procedures taken to explant the device, in accordance with Medtronic’s applicable Supplemental Limited Warranty. In addition, Medtronic recognizes that you may incur additional non-reimbursed expenses that are unique to your situation, and will work with you accordingly.

If there are expenses after your medical bills have been submitted and paid by your insurance (for example, Medicare and/or private insurance), please retain the relevant documentation (for example, itemized medical bills and the matching insurance payments statement, or parking receipts related to the surgery). For assistance or questions related to reimbursement, contact Medtronic Patient Services at 1-800-510-6735.

As always, please contact us if you notice an increase in your pain.

Sincerely,

[Physician name]
Dear [Patient Name]:

Medtronic, Inc., the manufacturer of your implantable pump, has recently informed us of a pump reliability concern. The motor component within your pump may stall and could result in decreased amount of the drug being delivered or not being delivered at all through the catheter. Although the chance of this happening to your pump is rather low, if it occurs, it could cause drug delivery to stop abruptly, resulting in loss of therapy, return of your underlying symptoms, and symptoms of drug underinfusion or withdrawal which can in the most severe cases be fatal if not treated promptly and effectively.

As you may know, the pump that delivers your therapy has an average battery life of 5 to 7 years. Because your pump is nearing its normal end of battery life, you may wish to consider having the pump replaced now. Please contact our office at XXX-XXX-XXXX. As always, if you have any question or concerns, please contact our office.

To address the impact of any inconvenience that you may experience related to early replacement surgery, Medtronic will reimburse you up to $1,000 of reasonable, non-reimbursed expenses incurred in connection with surgical procedures taken to explant the device, in accordance with Medtronic’s applicable Supplemental Limited Warranty. In addition, Medtronic recognizes that you may incur additional non-reimbursed expenses that are unique to your situation, and will work with you accordingly.

If there are expenses after your medical bills have been submitted and paid by your insurance (for example, Medicare and/or private insurance), please retain the relevant documentation (for example, itemized medical bills and the matching insurance payments statement, or parking receipts related to the surgery). For assistance or questions related to reimbursement, contact Medtronic Patient Services at 1-800-510-6735.

In the meantime, please continue to watch for the signs and symptoms of baclofen withdrawal. Early symptoms of abrupt withdrawal from intrathecal baclofen may include high fever, itching, low blow pressure, tingling sensations, altered mental status, return of baseline spasticity, and muscle rigidity. As always, it is very important that you contact us right away if you experience any of the above symptoms.

We look forward to hearing from you soon.

Sincerely,

[Physician name]
Procedure 8.4: Suspected Pump Underinfusion

Patient Symptom and Possible Cause

If the pump has underinfused by more than 25% of the expected volume (there is more drug in the reservoir than expected), and possible occlusion of implanted system components has been eliminated, the pump may not be operating properly. To confirm pump function, conduct a roller study using this procedure.

Troubleshooting Procedure

Review the following procedure carefully.

1. X-ray the pump to determine the location of the pump roller (overexposing the film will make the roller more visible). Several attempts may be necessary to visualize the roller (Figure 8-1).

Figure 8-1
Pump Roller Rotation

Figure 8-2
X-Ray of Pump
2. Calculate the amount of a bolus, in microliters (µL), that will move the roller 90°. Use the formula in Table 8-7.

<table>
<thead>
<tr>
<th>Table 8-7 Calculation for Moving Pump Roller 90°</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. <strong>Determine the calibration constant</strong> from the Pump Status Screen or patient’s Implanted Device Identification card.</td>
</tr>
</tbody>
</table>
| b. **Divide 1800 by the calibration constant.**  
The result is the volume in µL required to move the roller 90°.  
\[ \frac{1800}{\text{Cal Constant}} = \mu\text{L} \] |
| c. **Program the amount calculated (µL) using the above formula; OR** |
| d. **To obtain the bolus dose expressed in the present metrology, multiply the formula’s result (in µL) by the concentration, divided by 1000.**  
\[ \mu\text{L} \times \text{(drug concentration/mL)} = \text{Dose in Present Metrology} \]  
\[ \frac{\mu\text{L}}{1000 \mu\text{L/mL}} \] |
| e. **The pump will operate for approximately 45 seconds to deliver a bolus that will turn the roller 90°.** |

3. X-ray the pump and determine the new position of the pump’s roller. The pump’s roller should have moved 90°. Fluoroscopy can be used to visualize the pump as it moves to its new position (Figure 8-2).

4. If there is no roller movement, or less than 90° of movement, the device may be stalled. Contact Medtronic Technical Services or your local Medtronic Sales Specialist.

5. If the roller shows proper movement, make certain there are no occlusions in the catheter system. Refer to Procedure 8.2 or 8.3.

**WARNING**

Programming a bolus could lead to drug overdose. Therefore, caution must be used when calculating and programming all bolus doses.
If a patient receiving ITB™ Therapy (Intrathecal Baclofen Therapy) presents with the signs and symptoms suggestive of baclofen withdrawal (above), the following approach is consistent with that suggested by a panel of therapy-experienced clinicians convened to explore this issue:

1. Immediately contact a physician experienced in ITB Therapy, preferably the physician managing the therapy for the patient in question; follow the recommendations of this physician. This step is important even if the patient’s signs and symptoms seem mild.

2. If an ITB Therapy physician is unavailable, consider instituting one or more of the following options, unless otherwise contraindicated:
   - high-dose oral* or enteral baclofen
   - restoration of intrathecal baclofen infusion
   - intravenous benzodiazepines by continuous or intermittent infusion, titrating the dosage until the desired therapeutic effect is achieved

   *Note: Oral baclofen should not be relied upon as the sole treatment for intrathecal baclofen withdrawal syndrome.

Abrupt withdrawal of intrathecal baclofen, regardless of the cause, has, in rare cases, resulted in a life-threatening syndrome that included high fever, altered mental status, exaggerated rebound spasticity and muscle rigidity that progressed to rhabdomyolysis, multiple organ-system failure, and death.

All patients receiving ITB Therapy are potentially at risk. Some clinical characteristics of the advanced intrathecal baclofen withdrawal syndrome may resemble autonomic dysreflexia, sepsis, malignant hyperthermia, and neuroleptic-malignant syndrome. A rapid and accurate diagnosis is important in an emergency room or intensive care setting before initiating treatment in order to prevent the potentially life-threatening central nervous and systemic effects of intrathecal baclofen withdrawal.

The physician experienced with ITB Therapy should expeditiously attempt device troubleshooting. This may include, but is not limited to:

- interrogation of the pump status using the Medtronic pump programmer
- radiologic examination of the pump and catheter system
- a pump refill procedure with the appropriate concentration of baclofen
- system troubleshooting procedures to determine the cause of ITB Therapy interruption
- surgical repair, revision, or replacement of system components

Baclofen withdrawal has been identified during post-approval use of Lioresal Intrathecal. Because this reaction is reported spontaneously from a population of uncertain size, it is not possible to reliably estimate the frequency.

Refer to the drug manufacturer’s package insert for a complete list of indications, contraindications, warnings, precautions, adverse events, and dosage and administration information.


Lioresal® is a registered trademark of Novartis Pharmaceuticals Corporation.
Lioresal® Intrathecal (baclofen injection) Overdose

In the U.S. emergency technical support is available 24 hours/day for clinicians managing patients with Medtronic SynchroMed® Infusion System implants: 800-707-0933. In other world areas contact your Medtronic representative.

Refer to the drug manufacturer's package insert for a complete list of indications, contraindications, warnings, precautions, adverse events, and dosage and administration information.


Lioresal® is a registered trademark of Novartis Pharmaceuticals Corporation.

EMERGENCY PROCEDURE

Symptoms of Overdose
Drowsiness, lightheadedness, dizziness, somnolence, respiratory depression, seizures, rostral progression of hypotonia and loss of consciousness progressing to coma.

There is no specific antidote for treating overdoses of Lioresal Intrathecal. However, anecdotal reports suggest that intravenous physostigmine may reverse central side effects, notably drowsiness and respiratory depression.²

Medtronic SynchroMed Infusion System
The SynchroMed Infusion System consists of an implantable programmable pump, intraspinal catheter and pump programmer. The pump is implanted in the lower abdomen and dispenses medication from the pump's reservoir through the catheter to the intrathecal or epidural space. Some pumps are equipped with a catheter access port that bypasses the pump reservoir, permitting direct catheter access to the intrathecal or epidural space.

Suggested Treatment for Intrathecal Baclofen Overdose

| Maintain Airway/Breathing/Circulation. |
| Intubation and respiratory support may be necessary. |
| Empty pump reservoir to stop drug flow (see right). |
| Record amount withdrawn. |

Administer physostigmine if not contraindicated.

Adult Dosage: 0.5 to 1.0 mg IM or IV @ slow controlled rate of not >1mg/min.
(May repeat every 10-30 min. if desired patient response is not obtained.)
Pediatric Dosage: 0.02 mg/kg IM or IV, not >0.5 mg/min. May repeat every 5-10 min. up to 2 mg max.

If not contraindicated, withdraw 30-40 mL CSF by lumbar puncture or through the catheter access port to reduce baclofen concentration in the CSF.
For instructions on how to withdraw CSF through the catheter access port, please contact Medtronic Technical Services. In the U.S. call 1-800-707-0933.
In other world areas contact your Medtronic representative.

Notify patient’s ITB™ Therapy Physician (see right).

Continue to monitor closely for symptom recurrence.

Empty pump reservoir to stop drug flow (see right).

Record amount withdrawn.

Maintain Airway/Breathing/Circulation.

Intubation and respiratory support may be necessary.

Locate the pump (right or left abdomen) by palpation. Pump diameter is approximately 3 in./7 cm. The reservoir fill port is located in the CENTER of the pump.

The reservoir fill port is located in the CENTER of the pump.

Prepare injection site by cleansing area using an antiseptic agent; allow skin to dry.

Locate reservoir fill port and insert needle through skin. Enter the port's septum until the needle touches the metal needle stop. If you encounter resistance during needle insertion, reassess placement. Do not force the needle; use of excessive force may damage the needle.

Withdraw fluid from reservoir using negative pressure. Empty reservoir until large air bubbles are apparent in syringe.

Maintain negative pressure while removing needle and attached syringe together from port septum and skin.

Record amount of fluid emptied from reservoir in patient chart.

For instructions on how to withdraw CSF through the catheter access port, please contact Medtronic Technical Services. In the U.S. call 1-800-707-0933.
In other world areas contact your Medtronic representative.

Contact Information
ITB Therapy Physician

Name: ____________________________ Phone: ____________________________
City: ____________________________ State: ____________________________

Medtronic SynchroMed Pump Descriptions

<table>
<thead>
<tr>
<th>Pump Name/Model</th>
<th>Catheter Access Port?</th>
<th>Reservoir Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>SynchroMed II 8637-40</td>
<td>Yes, funnel-shaped</td>
<td>40 mL</td>
</tr>
<tr>
<td>SynchroMed II 8637-20</td>
<td>Yes, funnel-shaped</td>
<td>20 mL</td>
</tr>
<tr>
<td>SynchroMed EL 8627-18, 8627L-18*</td>
<td>No</td>
<td>18 mL</td>
</tr>
<tr>
<td>SynchroMed EL 8626-18, 8626L-18*</td>
<td>Yes, screened</td>
<td>18 mL</td>
</tr>
<tr>
<td>SynchroMed EL 8626-10, 8626L-10*</td>
<td>No</td>
<td>10 mL</td>
</tr>
<tr>
<td>SynchroMed 8618-18, 8618L-18*</td>
<td>Yes, not screened</td>
<td>18 mL</td>
</tr>
<tr>
<td>SynchroMed 8617-18, 8617L-18*</td>
<td>Yes, screened</td>
<td>18 mL</td>
</tr>
<tr>
<td>SynchroMed 8616-18</td>
<td>Yes, screened</td>
<td>18 mL</td>
</tr>
<tr>
<td>SynchroMed 8616-10</td>
<td>No</td>
<td>10 mL</td>
</tr>
</tbody>
</table>

Suggested Treatment for Intrathecal Baclofen Overdose

<table>
<thead>
<tr>
<th>Equipment</th>
</tr>
</thead>
<tbody>
<tr>
<td>• 22-gauge or smaller needle (1.5 in./3.8 cm or 2 in./5.1 cm)</td>
</tr>
<tr>
<td>• 20 mL luer-lock syringe</td>
</tr>
<tr>
<td>• antiseptic agent</td>
</tr>
</tbody>
</table>

1. Locate the pump (right or left abdomen) by palpation. Pump diameter is approximately 3 in./7 cm. The reservoir fill port is located in the CENTER of the pump.

2. Prepare injection site by cleansing area using an antiseptic agent; allow skin to dry.

3. Locate reservoir fill port and insert needle through skin. Enter the port's septum until the needle touches the metal needle stop. If you encounter resistance during needle insertion, reassess placement. Do not force the needle; use of excessive force may damage the needle.

4. Withdraw fluid from reservoir using negative pressure. Empty reservoir until large air bubbles are apparent in syringe.

5. Maintain negative pressure while removing needle and attached syringe together from port septum and skin.

6. Record amount of fluid emptied from reservoir in patient chart.

If not contraindicated, withdraw 30-40 mL CSF by lumbar puncture or through the catheter access port to reduce baclofen concentration in the CSF.

For instructions on how to withdraw CSF through the catheter access port, please contact Medtronic Technical Services. In the U.S. call 1-800-707-0933.
In other world areas contact your Medtronic representative.

Report incident to Medtronic, Inc. In the U.S. call 1-800-328-0810.
In other world areas contact your Medtronic representative.


UC200303503  EN  NP5676EN  PN221500-101
INDICATIONS,
DRUG STABILITY, AND
EMERGENCY PROCEDURES
SynchroMed® and IsoMed® implantable infusion systems

Reference manual
Rx only
Refer to the appropriate information for prescribers booklet for contraindications, warnings, precautions, adverse events summary, individualization of treatment, patient selection, use in specific populations, and component disposal.
Refer to the device implant manual for device description, package contents, device specifications, and instructions for use.

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</table>
Indications

Physicians prescribing the SynchroMed II, SynchroMed, or SynchroMed EL Infusion Systems or the IsoMed Constant-Flow Infusion System for use with the drugs listed in Table 1 must be familiar with the indications, contraindications, warnings, precautions, adverse events, dosage and administration information, and screening procedures described in the drug labeling. Each system includes (at a minimum) a pump and a catheter.

Table 1. Drug indications for Medtronic implantable infusion systems.

<table>
<thead>
<tr>
<th>Drugs approved for use with infusion system</th>
<th>SynchroMed II</th>
<th>SynchroMed and SynchroMed EL</th>
<th>IsoMed</th>
</tr>
</thead>
<tbody>
<tr>
<td>The chronic epidural/intrathecal infusion of preservative-free morphine sulfate sterile solution in the treatment of chronic intractable pain. A 0.9% solution of preservative-free sodium chloride injection, USP, can be used to achieve the physician-prescribed concentration of preservative-free morphine sulfate sterile solution.</td>
<td>X</td>
<td>X</td>
<td>X⁵</td>
</tr>
<tr>
<td>The chronic intravascular infusion of flouxuridine (FUDR) for the treatment of primary or metastatic cancer. Bacteriostatic water or preservative-free sterile saline (USP) can be used to achieve the physician-prescribed concentration of chemotherapy drugs or to flush the pump reservoir. Saline or heparinized physiological saline (unless contraindicated) may be used during an interruption in chemotherapy to maintain pump and catheter patency.</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
</tbody>
</table>
The chronic intravascular infusion of methotrexate for the treatment of primary or metastatic cancer. Bacteriostatic water or preservative-free sterile saline (USP) can be used to achieve the physician prescribed concentration of chemotherapy drugs or to flush the pump reservoir. Saline or heparinized physiological saline (unless contraindicated) may be used during an interruption in chemotherapy to maintain pump and catheter patency.

The chronic intrathecal infusion of preservative-free ziconotide sterile solution for the management of severe chronic pain. A 0.9% solution of preservative-free sodium chloride injection, USP, can only be used with preservative-free ziconotide sterile solution after the initial fill of the pump with this drug.

The chronic intrathecal infusion of Lioresal Intrathecal (baclofen injection) in the management of severe spasticity. A 0.9% solution of preservative-free sodium chloride injection, USP, can be used to achieve the physician-prescribed concentration of Lioresal Intrathecal (baclofen injection).

### Table 1. Drug indications for Medtronic implantable infusion systems.

<table>
<thead>
<tr>
<th>Drugs approved for use with infusion systema</th>
<th>SynchroMed II</th>
<th>SynchroMed and SynchroMed EL</th>
<th>IsoMed</th>
</tr>
</thead>
<tbody>
<tr>
<td>The chronic intravascular infusion of methotrexate for the treatment of primary or metastatic cancer. Bacteriostatic water or preservative-free sterile saline (USP) can be used to achieve the physician prescribed concentration of chemotherapy drugs or to flush the pump reservoir. Saline or heparinized physiological saline (unless contraindicated) may be used during an interruption in chemotherapy to maintain pump and catheter patency.</td>
<td>X</td>
<td>X</td>
<td>—</td>
</tr>
<tr>
<td>The chronic intrathecal infusion of preservative-free ziconotide sterile solution for the management of severe chronic pain. A 0.9% solution of preservative-free sodium chloride injection, USP, can only be used with preservative-free ziconotide sterile solution after the initial fill of the pump with this drug.</td>
<td>X</td>
<td>X</td>
<td>—</td>
</tr>
<tr>
<td>The chronic intrathecal infusion of Lioresal Intrathecal (baclofen injection) in the management of severe spasticity. A 0.9% solution of preservative-free sodium chloride injection, USP, can be used to achieve the physician-prescribed concentration of Lioresal Intrathecal (baclofen injection).</td>
<td>X</td>
<td>X</td>
<td>—</td>
</tr>
</tbody>
</table>

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The chronic intravascular infusion of doxorubicin or cisplatin for the treatment of primary or metastatic cancer. Bacteriostatic water or preservative-free sterile saline (USP) can be used to achieve the physician prescribed concentration of chemotherapy drugs or to flush the pump reservoir. Saline or heparinized physiological saline (unless contraindicated) may be used during an interruption in chemotherapy to maintain pump and catheter patency.

The intravenous infusion of clindamycin for the treatment of osteomyelitis.

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### Table 1. Drug indications for Medtronic implantable infusion systems.

<table>
<thead>
<tr>
<th>Drugs approved for use with infusion systema</th>
<th>SynchroMed II</th>
<th>SynchroMed and SynchroMed EL</th>
<th>IsoMed</th>
</tr>
</thead>
<tbody>
<tr>
<td>The chronic intravascular infusion of doxorubicin or cisplatin for the treatment of primary or metastatic cancer.</td>
<td>—</td>
<td>X</td>
<td>—</td>
</tr>
<tr>
<td>The intravenous infusion of clindamycin for the treatment of osteomyelitis.</td>
<td>—</td>
<td>X</td>
<td>—</td>
</tr>
</tbody>
</table>

---

* a Refer to the appropriate drug labeling for a complete list of indications, contraindications, warnings, precautions, dosage and administration information, and screening procedures.
* b IsoMed is approved only for intrathecal infusion of preservative-free morphine sulfate sterile solution.
* X Specific pump is approved for use with drug.
* — Specific pump is not approved for use with drug.
Drug stability

Testing has indicated that the drugs in Table 2 are stable and compatible with the infusion systems listed in the table. Refer to the appropriate drug labeling for complete prescribing information, including indications, contraindications, warnings, precautions, and adverse events.

### Table 2. Stability of drugs approved for use with Medtronic implantable infusion systems.

<table>
<thead>
<tr>
<th>Drug</th>
<th>SynchroMed II</th>
<th>SynchroMed EL</th>
<th>IsoMed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cisplatin (1 mg/mL)</td>
<td>—</td>
<td>7 days</td>
<td>—</td>
</tr>
<tr>
<td>Clindamycin (70 mg/mL)</td>
<td>—</td>
<td>28 days</td>
<td>—</td>
</tr>
<tr>
<td>Doxorubicin (5 mg/mL)</td>
<td>—</td>
<td>14 days</td>
<td>—</td>
</tr>
<tr>
<td>Fluorouracil (FUDR) (20 mg/mL)</td>
<td>56 days</td>
<td>28 days</td>
<td>27 days</td>
</tr>
<tr>
<td>Lioresal Intrathecal (baclofen injection) (0.5 mg/mL) (2 mg/mL)</td>
<td>180 days</td>
<td>90 days</td>
<td>—</td>
</tr>
<tr>
<td>Methotrexate (5 mg/mL)</td>
<td>56 days</td>
<td>28 days</td>
<td>—</td>
</tr>
<tr>
<td>Morphine sulfate sterile solution (preservative-free) (25 mg/mL)</td>
<td>180 days</td>
<td>90 days</td>
<td>90 days</td>
</tr>
<tr>
<td>Ziconotide sterile solution (preservative-free)</td>
<td>Initial fill</td>
<td>Refill</td>
<td>Initial fill</td>
</tr>
<tr>
<td>25 µg/mL, undiluted</td>
<td>14 days</td>
<td>60 days</td>
<td>14 days</td>
</tr>
<tr>
<td>100 µg/mL, undiluted</td>
<td>*</td>
<td>60 days</td>
<td>*</td>
</tr>
<tr>
<td>100 µg/mL, diluted</td>
<td>*</td>
<td>40 days</td>
<td>*</td>
</tr>
</tbody>
</table>

* Stability is defined as 90% of initial concentration.
* For a pump that has not been previously filled with preservative-free ziconotide sterile solution, only the undiluted 25 µg/mL formulation of preservative-free ziconotide sterile solution can be used for the initial pump fill. Refill of the pump with this drug should be completed within 14 days to avoid underdosing the patient. At initial fill of a new pump, some of the drug is lost due to two factors that do not occur upon subsequent refills: adsorption on internal device surfaces, such as titanium, and by dilution in the residual space of the device. Refer to the drug labeling for additional information.
* — Drug is not approved for use with this specific pump.
* — Formulation is not applicable for the initial pump fill.
Emergency procedures

**Morphine intrathecal/epidural overdose**

Consult the patient's medical record or with the patient's physician to confirm the drug or drug concentration within the pump reservoir.

**Symptoms**

Respiratory depression with or without concomitant central nervous system depression (i.e., dizziness, sedation, euphoria, anxiety, seizures, respiratory arrest).
Actions

Maintain airway/breathing/circulation. Respiratory resuscitation and intubation may be necessary.

Give naloxone (Narcan) 0.4 – 2 mg intravenously.1,2,3

If not contraindicated, withdraw 30 – 40 mL of CSF through the catheter access port or by lumbar puncture to reduce CSF morphine concentration. Use only a 24-gauge4 or smaller, 1.5 or 2.0 inch (3.8 or 5.1 cm) needle for withdrawal from the catheter access port.

Empty pump reservoir to stop drug flow. Record amount withdrawn.

Response No Response

Continue to monitor closely for symptom recurrence. Since the duration of the effect of IV naloxone (Narcan) is shorter than the effect of intrathecal/epidural morphine, repeated administration may be necessary.1

Continue to perform life-sustaining measures.

No Recurrence Recurrence

Repeat naloxone (Narcan) every 2 – 3 minutes to maintain adequate respiration.1,2

For continuous IV infusion see naloxone (Narcan) package insert.2

If no response is observed after 10 mg of naloxone (Narcan), the diagnosis of narcotic-induced toxicity should be questioned.1,2

Call physician.

Figure 1. Morphine intrathecal/epidural overdose emergency procedures.

1 Infumorph (Preservative-free morphine sulfate sterile solution) manufacturer’s package insert (Wyeth-Ayerst).
2 Narcan (naloxone hydrochloride) manufacturer’s package insert (DuPont).
3 Refer to the drug manufacturer’s package insert for a complete list of indications, contraindications, warnings, precautions, adverse events, and dosage and administration information.
4 Use a 25-gauge needle for withdrawal from a SynchroMed or SynchroMed EL catheter access port. Use a 24- or 25-gauge needle for withdrawal from a SynchroMed II or IsoMed catheter access port.

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Lioresal Intrathecal (baclofen injection) overdose

Consult the patient's medical record or with the patient's physician to confirm the drug or drug concentration within the pump reservoir.

Symptoms
Drowsiness, lightheadedness, dizziness, somnolence, respiratory depression, seizures, rostral progression of hypotonia, and loss of consciousness progressing to coma.

There is no specific antidote for treating overdoses of Lioresal Intrathecal (baclofen injection). However, anecdotal reports suggest that intravenous physostigmine may reverse central side effects, notably drowsiness and respiratory depression.
Actions

Maintain airway/breathing/circulation.  
Intubation and respiratory support may be necessary.

Empty pump reservoir to stop drug flow.  
Record amount withdrawn.

Administer physostigmine if not contraindicated.  

**Adult dosage:** 0.5 – 1.0 mg intramuscularly or intravenously no more than 1 mg per minute. The dosage may be repeated at 10- to 30-minute intervals until a therapeutic effect is obtained.  

**Pediatric dosage:** 0.02 mg/kg intramuscularly or intravenously no 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.

If not contraindicated, withdraw 30 – 40 mL CSF by lumbar puncture or through the catheter access port to reduce the concentration of baclofen in the CSF. Use only a 24-gauge or smaller, 1.5 or 2.0 inch (3.8 or 5.1 cm) needle for withdrawal from the catheter access port.

Notify patient’s physician managing Lioresal Intrathecal (baclofen injection) therapy.

Continue to monitor closely for symptom recurrence.

Report incident to Medtronic, Inc.

**Figure 2.** Lioresal Intrathecal (baclofen injection) overdose emergency procedures.

1 Refer to the drug manufacturer’s package insert for a complete list of indications, contraindications, warnings, precautions, adverse events, and dosage and administration information.


3 Use a 25-gauge needle for withdrawal from a SynchroMed or SynchroMed EL catheter access port. Use a 24- or 25-gauge needle for withdrawal from a SynchroMed II or IsoMed catheter access port.
Lioresal Intrathecal (baclofen injection) underdose/withdrawal

Consult the patient’s medical record or with the patient’s physician to confirm the drug or drug concentration within the pump reservoir.

Symptoms of underdose
Pruritus without rash, hypotension, paresthesia, fever, and altered mental state.

Symptoms of withdrawal
Exaggerated rebound spasticity and muscle rigidity, rhabdomyolysis, and multiple organ failure. The condition may resemble autonomic dysreflexia, sepsis, malignant hyperthermia, and neuroleptic-malignant syndrome.

Actions

- Initiate life-sustaining measures if indicated.

If a patient receiving Lioresal Intrathecal (baclofen injection) presents with the signs and symptoms suggestive of Lioresal Intrathecal (baclofen injection) withdrawal (above), the following is consistent with that suggested by a panel of therapy-experienced clinicians convened to explore this issue1,2:

1. Immediately contact a physician experienced in Lioresal Intrathecal (baclofen injection), preferably the physician managing the therapy for the patient in question; follow the recommendations of this physician. This step is important even if the patient’s signs and symptoms seem mild.

2. If a physician experienced in Lioresal Intrathecal (baclofen injection) is unavailable, consider instituting one or more of the following options, unless otherwise contraindicated:
   - high-dose oral* or enteral baclofen
   - restoration of Lioresal Intrathecal (baclofen injection) infusion
   - intravenous benzodiazepines by continuous or intermittent infusion, titrating the dosage until the desired therapeutic effect is achieved

*Note: Oral baclofen should not be relied upon as the sole treatment for Lioresal Intrathecal (baclofen injection) withdrawal syndrome.

- Report incident to Medtronic, Inc.

Figure 3. Lioresal Intrathecal (baclofen injection) underdose/withdrawal emergency procedures.

1 Refer to the drug manufacturer’s package insert for a complete list of indications, contraindications, warnings, precautions, adverse events, and dosage and administration information.


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Emergency procedure to empty the pump reservoir

**Equipment**
- 22-gauge needle
- 20-mL syringe(s)
- 3-way stopcock
- Antiseptic agent

1. Locate the pump by palpation. The reservoir fill port is located in the CENTER of the pump.
2. Prepare the injection site by cleansing the area using antiseptic agent.
3. Gently insert the 22-gauge needle into the center of the reservoir fill port septum until the needle touches the needle stop. If the clinician encounters resistance during needle insertion, the clinician should reassess placement. Do not force the needle. Hitting metal or the feel of abnormal resistance during the procedure may be an indication that the needle is not in the center of the reservoir fill port septum.

⚠️ **Cautions:**
- The IsoMed pump reservoir contents are under significant pressure. To prevent the reservoir contents from being ejected, do not use an open syringe when emptying the pump.
- When removing a vesicant or cytotoxic drug, care must be taken to prevent spillage or leakage of the drug into adjacent tissue.

4. If desired, use a 3-way stopcock. Withdraw fluid from the pump reservoir using passive backflow and gentle negative pressure. Empty the pump reservoir until back-flow has stopped and wait five seconds to ensure all fluid is removed and the pump reservoir is empty. Depending on pump reservoir volume, more than one syringe may be needed to empty the pump.
5. Remove the needle from the reservoir fill port.
6. Record in the patient chart the amount of fluid emptied from the pump reservoir.

**Technical Services**

For additional information, contact Medtronic Technical Services at 1-800-328-0810.