REPUBLIC OF LEBANON
MINISTRY OF PUBLIC HEALTH
The Director General

الجمهورية اللبنانية
وزارة الصحة العامة
المدير العام

رقم المحفوظات: ٢٨/ ٥٠
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جانب نقيب المستشفيات الخاصة في لبنان

الموضوع: إشعار بمتابعة جهاز طبي مغروس

General-purpose implantable infusion pump, SynchroMed II and SynchroMed EL Implantable Drug Pumps and Refill Kits

الجهاز المعني بالمتابعة:

- General-purpose implantable infusion pump, SynchroMed II and SynchroMed EL Implantable Drug Pumps and Refill Kits
- Trade Mark: Medtronic Limited
- Local Representative: Tamer Frères/ Prime Medical

بناء على التوصية الصادرة عن الشركة المصنعة والتي تشير الى وجود خلل في عمل الجهاز المذكور أعلاه مما يؤثر على سلامة المريض، نرجو منكم تعميم هذه النشرة على جميع المستشفيات المعنية.

مرفق ربطا:

- التوصية الصادرة عن الشركة المصنعة

يبلغ:

- دائرة البرامج والمشاريع
- المستشفيات الحكومية
- المحفوظات

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Medtronic

Urgent Field Safety Notice

SynchroMed® Implantable Infusion Pump Priming Bolus

June 2013

Medtronic Reference: FA573

Dear Healthcare Professional,

This letter provides important safety information and patient management recommendations regarding the unintended delivery of drug during the priming bolus function for the SynchroMed® implantable infusion pump. This unintended delivery of drug can contribute to patient overdose or underdose symptoms which may be clinically relevant. Please see the attached **Potential Impact of Drug Mixing During Priming Bolus** for more information.

Background and nature of the issue:
The SynchroMed priming bolus function is intended to quickly advance drug from the pump reservoir to the catheter tip to allow for therapy initiation while the patient remains under medical supervision. Although drug is not intended to be delivered to the cerebrospinal fluid (CSF) during the priming bolus, mixing of the drug and non-drug (sterile water/CSF) fluids occurs at the high infusion rates used during a priming bolus. Mixing results in the unintended delivery of drug prior to the end of the programmed bolus, as well as dilution of some of the drug remaining in the catheter at the end of the bolus. Patients will receive unintended drug at a high rate of infusion in the CSF during the priming bolus, and a period of reduced concentration of drug will occur following the priming bolus.

Medtronic has performed preliminary bench testing of pumps and catheters to characterize the extent of drug mixing during a priming bolus. It is clear that the amount of drug delivered during the priming bolus procedure is related to the concentration of the drug; however clinical relevance is not fully understood. As part of the evaluation of the priming bolus, Medtronic also reviewed previously reported adverse events of overdose, underdose, and death following an infusion system implant or revision. Since drug mixing will occur any time the priming bolus is used with a SynchroMed pump, it is reasonable to expect that the resulting unintended drug delivery is a contributing factor to adverse events involving overdose and underdose. These adverse events will vary depending on the drug being infused, but could include lack of therapeutic effectiveness, confusion or altered mental state, sleepiness, nausea, respiratory depression, coma or death. Medtronic has been unable to establish a definitive causal relationship to priming bolus due to a number of other potential contributing factors including: drug dosage, the patient medical history, and the concomitant use of other drugs, such as oral opioids and other central nervous system (CNS) depressants.

Recommendations for Patient Management and Monitoring after Initiation of Intrathecal Therapy:
Medtronic recommends following published guidance for managing all patients with intrathecal therapy, in addition to the following:

- Continue use of the priming bolus procedure to ensure that therapy is initiated while the patient is under medical supervision.
- Monitor all patients following start or restart of intrathecal therapy as recommended below. The post-procedure monitoring period will depend upon specific drug dose administered and patient co-morbidities.
    - Opioids - For patients initiated or reinitiated with intrathecal infusion of opioids, monitoring with pulse oximetry for a minimum of 24 hours or until they demonstrate stable neurological, respiratory and cardiac function in a facility equipped with emergency airway management, oxygen, naloxone for treatment of opioid overdose and other emergency services is

recommended. Please refer to additional instructions provided in the drug product labeling (including Infumorph®[1]) and published guidance.[2]

- Baclofen – Patients initiating or reinitiating an intrathecal infusion of baclofen should be monitored in a facility that provides experienced nursing observation, with the ability and personnel for emergency airway management and ventilator support readily available. Patients should be monitored for a minimum of 8 hours or until they demonstrate stable neurological, respiratory and cardiac function.
- Ziconotide – There are no labeling guidelines for patient monitoring after initiating or restarting ziconotide therapy.[3] Published guidance recommends an overnight admission.[2]

- Consider priming the pump prior to implant in the patient and before connection to the catheter (back table prime) to decrease the risk of overdose, especially in patients receiving higher concentration opioid drug solutions and low total daily dose.
- Educate caregivers and family members to recognize the signs and symptoms associated with intrathecal drug therapy complications.[2]
- Patients who are receiving intrathecal baclofen and who receive a catheter-only priming bolus with or without a CAP aspiration will take longer to reach full intended drug concentration. Dose titration may need to be supplemented with oral baclofen to treat spasticity until the optimal intrathecal dose is obtained.
- Physicians should advise patients to avoid using concomitant drugs that may cause respiratory or CNS depression while intrathecal therapy is being initiated or resumed.

The Competent Authority of your country has been notified of this action.

This notice needs to be passed on all those who need to be aware within your organization.

We deeply apologize for any disruption this may cause your practice. Please know, patient safety is our top priority. Feel free to contact us if you have any questions or concerns. We appreciate your time and attention to this important notification, and thank you for continuing to put your trust in Medtronic.

Sincerely,

BU Country Manager

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[1] Infumorph [package insert]. West-Ward Pharmaceuticals, Eatontown, NJ; September 2011. http://www.west-ward.com/images/files/package/Infumorph%20200&500%20PI.pdf. Accessed April 17, 2013.

[2] Deer, T. R., Prager, J., Levy, R., et. al. (2012), Polyanalgesic Consensus Conference—2012: Recommendations on Trialing for Intrathecal (Intraspinal) Drug Delivery: Report of an Interdisciplinary Expert Panel. *Neuromodulation: Technology at the Neural Interface*, 15: 467–482.

[3] http://dailymed.nlm.nih.gov/dailymed/lookup.cfm?setid=5449ca98-efb8-4c3b-8756-747b2349a472

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May 2013

Appendix 1: Potential Impact of Drug Mixing During Priming Bolus

Medtronic convened a panel of experts to review the initial data, and the following patient populations were identified as having increased risk:

- Opioid-naïve or opioid-sensitive patients undergoing new pump and catheter implants, especially those prescribed high concentration drug solutions at the lowest daily doses, are at increased risk of intrathecal drug overdose.
- Patients who are highly sensitive to baclofen and require low daily doses may experience effects of increased drug immediately following the priming bolus.
- For baclofen patients undergoing pump or catheter revision with or without a catheter access port (CAP) aspiration, a delay in achieving the intended therapeutic dose will occur and may result in temporary return of symptoms such as increased spasticity.

Note: Other clinically relevant patient populations may exist in addition to these examples.

The amount of drug delivered to a patient during a priming bolus is impacted by multiple factors, including the type of priming bolus (full system or catheter only prime), specific drug concentration, catheter length and diameter, priming volume, priming duration and patient characteristics. High concentration drugs combined with flow rates associated with priming bolus will increase the extent of mixing and the amount of drug delivered prior to the end of the priming bolus. For patients requiring a low daily dose, the amount of drug introduced during the priming bolus will represent a larger proportion of the intended daily dose with the potential for greater clinical effect. In addition, it may take longer for patients to receive the full intended dose if a catheter only prime is performed with or without a catheter access port (CAP) aspiration.

The following full system prime scenarios, while preliminary, indicate current understanding:

- A full prime of the pump and catheter (using current recommended protocol) with a post-prime flow rate at the lowest settings may result in a delivered dose in the range of ~100% of the intended daily dose during the priming bolus. While a priming bolus takes 20-30 minutes to complete, diluted drug may exit the distal tip of the catheter during the final three to seven minutes of the priming bolus. For patients using morphine at a concentration of 25 mg/ml receiving the lowest possible dose of morphine (1.2 mg/day using 0.048 ml/day flow rate) this may represent a bolus delivery in the range of 1.2 mg (~100% of the daily dose). For patients using morphine at a concentration of 10 mg/ml receiving the lowest possible dose of morphine with this concentration (0.5 mg /day using 0.048 ml/day flow rate) this may represent a bolus dose in the range of 0.5 mg.
- For patients receiving a more clinically common dosing regimen of 10 mg/ml and a therapeutic goal of 3 mg /day (using 0.300 ml/day flow rate) the patient may receive a bolus in the range of 0.75 mg (~25% of the intended daily dose) during the priming procedure.
- In the situation where the pump is fully primed prior to attachment of the catheter followed by a catheter only priming bolus (consistent with current recommended protocol) even with the highest concentration tested (25 mg/ml) the amount of drug delivered during the priming bolus is believed to be negligible.

The following scenarios, while preliminary, indicate the current understanding of catheter only prime scenarios (with or without CAP aspiration):

- A standard catheter only prime (using the current recommended protocol) with a post-prime flow rate of 0.048 ml/day may result in a 9 hour delay until drug delivery.
- For patients receiving a more clinically common dosing regimen using 0.300 ml/day, may result in up to a 3 hour delay until drug delivery.
- After 24 hours the intended daily dose is achieved in both of the above scenarios.

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Urgent Field Safety Notice
SynchroMed® Implantable Infusion Pump Internal Shorting

June 2013

Medtronic reference: FA574

Dear Healthcare Professional,

The purpose of this communication is to provide safety information and patient management recommendations related to the potential for electrical shorting internal to the SynchroMed infusion pump.

Nature of Device Issue:
Within the SynchroMed pump, feedthroughs are components that provide an electrically insulated path for current to flow from the electronic circuitry to the motor. An electrical short can occur when ions from the drug solution and humidity permeate through the drug pathway tubing inside the pump and interact with the feedthrough over time. An electrical short circuit in a feedthrough may present as a motor stall or low battery reset/alarm and lead to a loss of or reduction in therapy which may result in the return of underlying symptoms and/or withdrawal symptoms.

Scope and Likelihood of Issue:
All SynchroMed II and SynchroMed EL pumps can potentially be affected by this issue at any time throughout the life of the device, regardless of drugs used in the pump. The SynchroMed EL has been discontinued and based on Medtronic data, at least 90% of the remaining actively implanted SynchroMed EL pumps are near expected end of service.

Medtronic has assessed reports of internal feedthrough shorting in the SynchroMed II pump since its release in 2004. There have been 380 relevant product events from approximately 181,400 pump implants worldwide. Medtronic's analysis of returned products and reports data shows the cumulative failure probability for internal feedthrough shorting to be approximately 0.28% at 48 months and 0.69% at 84 months post implant.

Severity:
SynchroMed pump internal feedthrough shorts can lead to a loss of or reduction in therapy which may result in a return of underlying symptoms and/or withdrawal symptoms. Patients receiving intrathecal baclofen therapy are at risk for baclofen withdrawal syndrome, which can lead to a life threatening condition if not promptly and effectively treated. Surgical revision to replace or remove the pumps may be required for patients with pumps experiencing repeated motor stalls, Low Battery Resets (with or without Safe State), or a premature Elective Replacement Indicator.

How to Identify Pumps Potentially Affected:
For SynchroMed II, this issue may be exhibited as one or more of the following:

- Repeated motor stalls with recovery listed in the pump event log, not associated with temporary exposure to a magnetic field (e.g. MRI).
- Multiple "Reset - Low Battery" errors (critical alarm) listed in the pump event log. After a reset, the pump may change to "Safe State". While in Safe State, the pump does not deliver at a therapeutic rate.
- Premature Elective Replacement Indicator (non-critical alarm), which is one that occurs sooner than expected based on implant duration and flow rate.

For SynchroMed EL, this issue may be exhibited as one or both of the following:

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- Motor Stall as determined by rotor study
- Low battery alarm

Recommendations:

Medtronic does not recommend prophylactic replacement of SynchroMed II or SynchroMed EL pumps due to the estimated low occurrence rate, the presence of pump alarms, and the risks associated with replacement surgery. However, appropriate consideration should be given to individual patient needs.

If repeated short duration motor stalls, Low Battery Resets (with or without Safe State), or a premature Elective Replacement Indicator occur, replacement surgery should be scheduled for therapy continuation. Alternative medical management should be considered if appropriate.

Ongoing Patient Management Recommendations:

- Continue to monitor patients closely for the return of baseline symptoms. A return of baseline symptoms may potentially indicate pump failure.
- Inform patients about the importance of keeping their pump refill appointments and contacting their physician immediately if the pump alarm sounds or if they notice a change or return of symptoms. Remind patients to always carry their patient identification card.
- Reinforce with patients and caregivers information on the signs and symptoms of withdrawal due to therapy cessation, and the importance of contacting their healthcare provider immediately if the identified signs and symptoms appear.
- The SynchroMed II pump is designed with both critical and non-critical alarms.
  - Increase the critical alarm interval frequency. The critical alarm interval frequency may be changed to sound every 10 minutes.
  - Remind patients, their caregivers, and your appropriate staff members to be alert for pump alarms.
  - At implant or follow-up visits, perform an alarm test to provide an opportunity for patients and caregivers to hear and differentiate between the critical and non-critical pump alarms.
  - For patients with a Personal Therapy Manager (PTM), if there is an active alarm, the PTM will show an alarm code when a bolus is attempted.
  - Retrieve and check logs for critical alarm events when interrogating the SynchroMed II pump. Note that a motor stall with recovery is expected in the event log when the pump is exposed to a strong magnetic field, such as during an MRI. Medtronic Technical Services may be contacted for further assistance evaluating critical alarm events on logs.
- For the SynchroMed EL pump:
  - Remind patients, their caregivers, and your appropriate staff members to be alert for the low battery pump alarm.
  - For suspected motor stalls, perform a rotor study to confirm or rule out a motor stall.

The Competent Authority of your country has been notified of this action.
This notice needs to be passed on all those who need to be aware within your organization.

We deeply apologize for any disruption this may cause your practice. Please know, patient safety is our top priority. Feel free to contact us if you have any questions or concerns. We appreciate your time and attention to this important notification, and thank you for continuing to put your trust in Medtronic.

Sincerely,

BU Country Manager