

Medtronic

SynchroMed™

IsoMed™

8667(8667-20/8667-40)
Implantable infusion systems

Information for prescribers

 Rx only

CE 0123

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Note: Some product models may not be available in all geographies.

Information available for the system:

The information for prescribers manual provides information about contraindications, warnings, precautions, adverse events, sterilization, patient selection, individualization of treatment, and component disposal.

For customers in Japan, the appropriate package insert provides information about indications, safety, contraindications, warnings, precautions, and adverse events.

The indications, drug stability, and emergency procedures reference manual provides information about indications and related information.

The appropriate drug labeling provides information about indications, contraindications, warnings, precautions, dosage and administration information, and screening procedures.

The MRI guidelines provide information about any MRI conditions and MRI-specific contraindications, warnings, and precautions for MRI scans with the infusion system.

Product manuals, such as programming guides and implant manuals provide device descriptions, package contents, device specifications, product-specific warnings and precautions, and instructions for use.

! USA **The clinical summary provides information about the clinical study results for the infusion system.**

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Contraindications

Pump implantation - Implantation of the pump is contraindicated:

- in the presence of infection.
- when the pump cannot be implanted 2.5 cm or less from the surface of the skin.
- in patients whose body size is not sufficient to accept pump bulk and weight.

Intrathecal catheterization - Intrathecal catheterization is contraindicated:

- in the presence of known or suspected meningitis, ventriculitis, skin infection, bacteremia, and septicemia.
- in the presence of spinal anomalies that may complicate the implantation and fixation of a catheter for drug delivery.

Drugs - Contraindications relating to the use of the prescribed drug must be observed.

Drugs with preservatives - Drugs with preservatives are contraindicated when known to damage the SynchroMed Infusion System (eg, sodium metabisulfite).

Catheter access port kits - Medtronic catheter access port kits are contraindicated for all refill procedures.

Low pH - Drug formulations with pH ≤ 3 are known to damage the SynchroMed Infusion System and are contraindicated.

Refill kits - Medtronic refill kits are contraindicated for all catheter access port procedures.

Warnings

User instructions - Comply with all product instructions for initial preparation and filling, implantation, programming (if applicable), refilling, and accessing the catheter access port (if present) of the pump. Failure to comply with all instructions can lead to technical errors or improper use of implanted infusion pumps and result in additional surgical procedures, a return of underlying symptoms, drug withdrawal symptoms, or a clinically significant or fatal drug underdose or overdose.

Alcohol contact - Do not expose the catheter components to alcohol or solutions containing alcohol. Alcohol can damage the components. Component damage can result in drug or spinal fluid leakage into surrounding tissue and tissue damage or a loss of or change in therapy, which may lead to a return of underlying symptoms, drug withdrawal symptoms, or a clinically significant or fatal drug underdose or overdose. Damage to the components can require surgery to repair or replace the components.

Advancing drug to catheter tip - Do not inject drug directly into the catheter or through the catheter access port to advance drug to the catheter tip. Injecting through the catheter access port or injecting directly into the catheter to advance drug to the catheter tip can result in a clinically significant or fatal drug overdose.

Catheter aspiration - Before injecting fluids through the catheter access port, aspirate approximately 1 to 2 mL from the catheter. A significant amount of drug may be present in the catheter access port and catheter, and failure to remove the drug during catheter access port injections can result in a clinically significant or fatal drug overdose.

Contrast medium - When injecting contrast medium into the intraspinal space, use ONLY contrast medium indicated for intraspinal use. Using nonindicated contrast media can result in adverse events including, but not limited to, extreme pain, cramps, seizures, and death. Inject contrast medium through the catheter access port only.

Coagulopathies - Assess patients for intrathecal catheter implantation to assure that risks for increased or uncontrolled bleeding are not present and/or are managed optimally. Physicians should specifically investigate the following:

- Anatomical factors at or near the implant site (eg, vascular abnormalities, neoplasms, or other abnormalities)
- Underlying disorders of the coagulation cascade, platelet function, or platelet count (eg, hemophilia, Von Willebrand's disease, liver disease, or other medical conditions)
- The administration of any antiplatelet or anticoagulant medication (eg, aspirin, clopidogrel bisulfate, NSAIDs) in the preoperative or perioperative period
- Use of nutritional supplements (eg, St. John's Wort) that can impact coagulation

Any of those conditions or drugs could place a patient at an increased risk for intraoperative or postoperative bleeding.

The decision to proceed with implant rests on stratification of risks and benefits in a particular patient. The risks and benefits of any patient management strategy, such as discontinuing anticoagulation medication during screening and the surgical procedure, should be discussed with patients and their caregivers.

Drug first use - Do not use high-concentration drugs the first time a drug is used because of the unknown therapeutic window. Using high-concentration drugs in this case could result in a clinically significant or fatal drug overdose.

Drug incompatibility - Medtronic implantable infusion systems are only approved for use with specific drugs. Do not use:

- drugs or fluids that may contain preservatives, antimicrobials, or antioxidants or that exhibit chemical properties (such as $\text{pH} \leq 3$) that are not compatible with the infusion system.
- drugs or fluids that may break down over time and produce degradation products that are not compatible with the infusion system (eg, diamorphine and diacetylmorphine).
- drugs or drug mixtures that may precipitate in the pump and inhibit pump flow or occlude the catheter (eg, greater than approved concentrations).

Specialty formulations Medtronic SynchroMed and IsoMed infusion systems are only approved for the use with specific drugs. Nonindicated formulations (including admixtures, compounded drugs, and unapproved drug concentrations) have not been tested with the SynchroMed / IsoMed infusion system. Use of nonindicated drugs or fluids can result in increased risks to the patient, intermittent stalling, overinfusion, or failure of the infusion system. Infusion system failure, which requires surgical replacement to correct, would result in a loss or change in therapy, and may lead to fluctuations in symptom control, a return of underlying symptoms, drug withdrawal symptoms, or a clinically significant or fatal drug underdose or overdose.

Drug quality - Do not use a drug if sterility is questionable or if the drug is cloudy or contains visible particulates. Using such a drug may cause infection or component occlusion that inhibits drug delivery, resulting in a loss of or change in therapy, which may

lead to a return of underlying symptoms, drug withdrawal symptoms, or a clinically significant or fatal drug underdose, and require surgical revision or replacement.

Inflammatory mass at the catheter tip (symptoms) - An inflammatory mass that can result in serious neurological impairment, including paralysis, could occur at the tip of the implanted catheter. Patients on intraspinal opioid therapy should be monitored carefully at each visit for any new neurological signs or symptoms.

Physicians should routinely monitor patients receiving **opioids** for the following prodromal clinical signs or symptoms of inflammatory mass:

- Change in the character, quality, or intensity of pain
- Reports of new radicular pain, especially at or near the dermatomal level of the catheter tip
- Frequent or large escalations of the daily drug dose are required to maintain the analgesic effect
- Dose escalations alleviate increasing pain only temporarily

To prevent possible permanent neurological injury, physicians should immediately evaluate patients who develop the following signs or symptoms:

- New or different sensory symptoms (eg, numbness, tingling, burning, hyperesthesia, hyperalgesia)
- New, occasional, or intermittent bowel or bladder sphincter dysfunction
- New motor weakness, change in gait, or difficulty walking
- Any neurological symptoms or signs that differ from baseline (eg, reflex changes)

Physicians should routinely monitor patients receiving **intrathecal baclofen** as a sole agent for the following prodromal clinical signs or symptoms of inflammatory mass:

- Change in the character, quality, or intensity of spasticity
- Frequent or large escalations of the daily drug dose are required to maintain the antispastic effect
- Rapid dose escalations alleviate the increasing spasticity only temporarily

Incidence of reports of inflammatory mass in pain patients: An analysis of the observed inflammatory mass cases in the Product Surveillance Registry (PSR) from 2003 through April 2017 indicates an incidence of 0.59% (1 in 170 chance; one-sided upper 95% confidence bound = 0.78%) of inflammatory mass in patients ever implanted with an infusion system for the treatment of pain. Cumulative risk of inflammatory mass was 0.30% at 5 years and 0.93% at 10 years.

The risk of inflammatory mass occurrence appears to be cumulative over time and increases with higher concentrations of opioids. Literature reports and preclinical studies have shown that inflammatory mass has been associated with a wide range of doses and concentrations of opioids. No dose and/or concentration of morphine sulfate can be considered completely free of risk from inflammatory mass. Current available information does not definitively exclude other possible contributing factors such as other infusates, catheter design, or material.

Incidence of reports of inflammatory mass in spasticity patients: An analysis of the observed inflammatory mass cases in the Product Surveillance Registry (PSR) from 2003 through April 2017 indicates an incidence of 0.06% (1 in 1,667 chance; one-sided upper

95% confidence bound = 0.29%) of inflammatory mass in patients ever implanted with an infusion system for the treatment of spasticity. Cumulative risk of inflammatory mass was 0.00% at 5 years and 0.00% at 10 years. Cases of intrathecal mass at the tip of the implanted catheter leading to withdrawal symptoms have also been reported, most of them involving pharmacy compounded analgesic admixtures.

Physicians managing patients on ITB TherapySM (Intrathecal Baclofen Therapy) should use their medical judgment regarding the most appropriate monitoring specific to their patients' medical needs to identify prodromal clinical signs and symptoms for inflammatory mass, especially for a change in the character, quality, or intensity of spasticity. Patients receiving pharmacy-compounded drugs or baclofen admixtures that include opioids should also be monitored per the recommendations noted above for opioids.

Refer to "Adverse events summary" on page 18 for more information on recognition, treatment, and mitigation of inflammatory mass.

Intraspinal therapy - For intraspinal therapy, use ONLY a preservative-free sterile solution indicated for intraspinal use. Nonindicated fluids containing preservatives or endotoxins can be neurotoxic in intraspinal applications. Using nonindicated fluids can result in adverse events including, but not limited to, extreme pain, cramps, seizures, and death.

Overinfusion - Overinfusion is defined as the delivery of more drug volume than the programmed rate, exceeding the pump's flow rate accuracy specification. Pump reservoir contents aspirated during a refill procedure that are less than expected may indicate that the pump has overinfused. Overinfusion may or may not be associated with clinically relevant symptoms. When the pump delivers more drug volume than the programmed rate, patients may experience overdose symptoms, and the pump reservoir will deplete more quickly than expected. Patients may experience underdose or withdrawal symptoms if the drug is depleted prior to the scheduled refill date from an overinfusing pump. At each refill visit, question and examine the patient for signs and symptoms of overdose, underdose, and withdrawal.

The low reservoir alarm of an overinfusing pump will not sound if the pump reservoir is prematurely depleted. The low reservoir alarm is calculated from the pump's programmed delivery rate and is not a direct measurement of the actual drug volume in the pump reservoir. Multiple factors may increase the likelihood of overinfusion, including: nonindicated drug formulations, overfilling of the pump reservoir, operation of the pump with no fluid in the reservoir, catheter occlusion, and pump stops or motor stalls lasting more than 48 hours.

Refer to the appropriate drug labeling for specific drug underdose or overdose symptoms and methods of management. If overinfusion is strongly suspected, contact Medtronic. Reducing the dose and/or concentration is not recommended as a solution for overinfusion. If immediate discontinuation of therapy is clinically appropriate for the patient, program the pump to minimum rate mode, and aspirate any remaining drug from the reservoir. Five occurrences of overinfusion have been identified in Medtronic's prospective, long-term multi-center registry study (Product Surveillance Registry) as of January 2016, resulting in a rate estimate of less than 0.14% (approximately 1 in 700).

Pocket fill - If it is suspected or known that all or part of the drug was injected into the pocket during the refill procedure, monitor the patient closely for signs and symptoms of overdose in an appropriate facility for a sufficient amount of time or until the symptoms have resolved. Refer to "Emergency Procedures" in the indications, drug stability, and emergency procedures manual, the refill instructions for use, and the appropriate drug labeling for specific drug underdose and overdose symptoms and methods of management.

Priming bolus

Priming bolus (SynchroMed Pumps) - Mixing of drug and non-drug (sterile water/CSF) fluids occurs at the high flow rates used during a priming bolus. This mixing can result in patients receiving drug prior to the end of the priming bolus, as well as a period of reduced drug concentration following the priming bolus, and can lead to adverse events involving drug overdose, underdose, and withdrawal. These adverse events will vary depending on the drug being infused, and could include lack of therapeutic effectiveness, confusion or altered mental state, sleepiness, nausea, respiratory depression, coma or death. Refer to "Emergency Procedures" in the indications, drug stability, and emergency procedures manual and the appropriate drug labeling for specific drug underdose and overdose symptoms and actions. Follow these guidelines regarding priming bolus:

- Use the priming bolus procedure to ensure that therapy is initiated while the patient is under medical supervision.
- To reduce the risk of overdose during a priming bolus, consider priming the pump before connecting the catheter to the pump (back table prime) during an initial system implant or a pump replacement. Refer to the clinician programmer guide for information on how to program the priming bolus.
- For a full system priming bolus: Avoid high concentration drug solutions with a low total daily dose as the risk for overdose and underdose can be more pronounced.
- For a full system priming bolus: Priming bolus default parameters have been carefully selected based on extensive modeling and testing. To ensure optimal initiation of therapy, modifications to these values are not recommended.
- For a full system priming bolus: Based on the therapeutic index of the drug and the sensitivity of the patient, some individuals may need additional monitoring until the delivered drug reaches the intended concentration. Do not increase the programmed daily dose within the first 48 hours following a priming bolus as the delivered drug may not have reached the intended concentration during this time.
- Medtronic recommends monitoring patients after any priming bolus procedure involving intrathecal therapy.
 - **Opioids:** Patients should be monitored with pulse oximetry for a minimum of 24 hours in a facility equipped with emergency airway management, oxygen, naloxone for treatment of opioid overdose and other emergency services.
 - **Baclofen:** Patients 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 starting or restarting ziconotide therapy. Published guidance recommends an overnight admission.
- Educate caregivers and family members to recognize the signs and symptoms associated with intrathecal drug overdose, underdose, and withdrawal. Instruct them to contact the patient's physician if they notice any of these signs or symptoms and to seek emergency assistance as necessary.

The following patient populations were identified as having increased risk of adverse events from drug overdose and underdose:

- Elderly patients.
- Patients with compromised respiratory, renal, hepatic, or cardiac function.
- Patients exposed to other agents, such as systemic opioids, alcohol, sedatives, antihistaminics, or psychotropic drugs that can potentiate the central nervous system depressant effects of intrathecal morphine.
- Opioid-naïve or opioid-sensitive patients undergoing new pump and catheter implants, especially those prescribed high concentration drug solutions with low daily doses.
- Patients who are sensitive to baclofen and require low daily doses.
- For baclofen patients undergoing pump or catheter revision, a delay in achieving the intended therapeutic dose could occur and may result in temporary return of symptoms such as increased spasticity or baclofen withdrawal.

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

Physician training

Drug information - Refer to the appropriate drug labeling for indications, contraindications, warnings, precautions, dosage and administration information, and screening procedures. Refer to the appropriate drug labeling for specific drug underdose or overdose symptoms and methods of management. Failure to refer to the drug labeling can result in inappropriate patient selection and management, inadequate therapy, intolerable side effects, or a clinically significant or fatal drug underdose or overdose. Consider the possibility of a drug error if the patient experiences unusual side effects. Failure to do so can result in misdiagnosis of patient symptoms.

Implantation and system management - Implantation and ongoing system management must be performed by individuals trained in the operation and handling of the infusion system and must be in compliance with procedures described in the appropriate technical instructions. Inadequate training or failure to follow instructions can require surgical revision or replacement, and result in a clinically significant or fatal drug underdose or overdose.

Prescribing - Physicians must be familiar with the drug stability information listed in the indications, drug stability, and emergency procedures manual and must understand the dose relationship to drug concentration and flow rate before prescribing an infusion system. Failure to understand the relationships between concentration, flow rate, dose, and drug stability can result in a clinically significant or fatal drug underdose or overdose.

Patient activities and information

Activities involving exposure to high altitudes - Patients who live or engage in activities (eg, airline flights, hiking, or skiing in the mountains) at altitudes greater than 2,438 meters (8,000 feet) are exposed to lower air pressures. With continued exposure to lower air pressure, the flow rate of the pump may increase and then stabilize at the higher flow rate. In those circumstances where a potential increase in flow rate may pose a risk for a patient, the infusion prescription can be adjusted to offset the higher flow rate. In rare instances, while the patient is exposed to lower pressures, exposure to lower pressures can cause:

- the flow rate of the SynchroMed II Pump to exceed the programmed flow rate by more than 14.5%.
- the flow rate of the IsoMed Pump to exceed the expected flow rate by more than 25%.

Changes in drug concentration or pump programming can be considered for patients who will be exposed to lower pressures. Refer to the appropriate device implant manual for additional information.

Activities involving exposure to high temperatures - Patients should talk to their doctors before using hot tubs, hot showers, steam rooms, saunas, or tanning beds where the temperature is greater than 39 °C (102 °F). The flow rate of the pump will vary with body temperature. A significant increase in body temperature can result in overinfusion.

Activities requiring excessive twisting or stretching - Patients should avoid activities that put undue stress on the implanted components of the infusion system. Activities that include sudden, excessive, or repetitive bending, twisting, bouncing, or stretching can damage or dislodge components and require surgical revision or replacement. These activities can also kink or occlude the catheter, resulting in a loss of or change in therapy, which may lead to a return of underlying symptoms, drug withdrawal symptoms, or a clinically significant or fatal drug underdose.

Component manipulation by patient (twiddler's syndrome) - Patients should avoid manipulating or rubbing the pump or catheter through the skin. Manipulation can cause skin erosion, component damage, catheter disconnection, kinking, or dislodgement and result in drug or CSF leakage into surrounding tissue and tissue damage or a loss of or change in therapy, which may lead to a return of underlying symptoms, drug withdrawal symptoms, or a clinically significant or fatal drug underdose or overdose, and can require surgical revision or replacement.

Manipulation may also cause pump inversion, making it impossible to refill the pump.

Drug interaction and side effects - Inform patients of the appropriate 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 the signs and symptoms and to seek appropriate medical intervention can result in serious patient injury or death.

Drug underdose/overdose - Inform patients and caregivers of the signs and symptoms of a drug underdose and overdose. Inform patients and caregivers:

- to be aware and report any unusual signs or symptoms at any time during or after a refill or catheter access port procedure.

- to be alert for any burning sensations in the area of the pump pocket during their refill or catheter access port procedure.
- to especially watch for signs of underdose and overdose.
- to stay alert for signs or symptoms that may indicate changes to their prescribed drug concentration or programmed dose.
- to seek emergency assistance as necessary. For emergency procedures associated with drug underdose and overdose, refer to the refill kit or catheter access port kit manual or the indications, drug stability and emergency procedures manual.

Failure to recognize these signs and symptoms and to seek appropriate medical intervention can result in serious patient injury or death.

Elective Replacement Indicator (SynchroMed II Pump) - Inform patients that the SynchroMed II Pump has an Elective Replacement Indicator (ERI) that sounds when the pump is nearing End of Service (EOS). When the ERI sounds, patients must contact their physician to schedule a pump replacement. If the pump is not replaced after the ERI sounds, the pump will reach EOS after 90 days and the pump will stop. A stopped pump results in loss of therapy, which may lead to a return of underlying symptoms, drug withdrawal symptoms, or a clinically significant or fatal drug underdose.

Long-term catheter damage - Inform patients that the catheter is subject to wear. Over time, the component may fail and require surgical revision or replacement. Component failure can result in drug or CSF leakage into surrounding tissue and tissue damage or a loss of or change in therapy, which may lead to a return of underlying symptoms, drug withdrawal symptoms, or a clinically significant or fatal drug underdose or overdose.

Medical procedures - Patients should always inform health care professionals that they have an implanted pump before undergoing medical tests or procedures. Failure to inform health care professionals can result in procedural delays, patient injury, component damage that requires surgical revision or replacement, or a clinically significant or fatal underdose or overdose.

Patient travel - Patients should notify their clinicians of any travel plans. Clinicians need this information to coordinate patient care and pump refills and help prevent a loss of or change in therapy, which may lead to a return of underlying symptoms, drug withdrawal symptoms, or a clinically significant or fatal drug underdose.

Refill - Patients must return to the clinic for refills at the prescribed times. Failure to return to the clinic for refills at the prescribed times can result in the actual flow rate of the pump being less than expected, resulting in a loss of or change in therapy, which may lead to a return of underlying symptoms, drug withdrawal symptoms, or a clinically significant or fatal drug underdose. Failure to return at the prescribed times and allowing the pump reservoir to empty completely can also damage the pump, requiring surgical replacement.

Scuba diving or hyperbaric chambers - Patients should not dive below 10 meters of water or enter hyperbaric chambers above 2.0 atmospheres absolute (ATA). Pressures below 10 meters of water (or above 2.0 ATA) could damage the pump, requiring surgical replacement. To minimize damage to the pump when hyperbaric treatment is required, fill the pump to capacity using the appropriate refill kit and maintain the current infusion prescription prior to exposure to hyperbaric conditions. Before diving or using a hyperbaric chamber, patients should discuss the effects of high pressure with their physician. As pressure increases, pump flow decreases. Continuing to increase the pressure will

eventually result in a loss of or change in therapy, which may lead to a return of underlying symptoms, drug withdrawal symptoms, or a clinically significant or fatal drug underdose.


Electromagnetic interference

Electromagnetic interference - Electromagnetic interference (EMI) is a field of energy generated by equipment found in the home, work, medical, or public environments that is strong enough to interfere with pump function. The programmable pumps include features that provide protection from electromagnetic interference. Most electrical devices and magnets encountered in a normal day are unlikely to affect the operation of a pump; however, sources of strong electromagnetic interference can result in the following:

- **Patient injury**, from heating of the implanted pump resulting in damage to surrounding tissue.
- **System damage**, from electrical or mechanical effects that can cause inappropriate device responses or loss of device function, resulting in loss of or change in therapy, which may lead to a return of underlying symptoms, drug withdrawal symptoms, or a clinically significant or fatal drug overdose or underdose.
- **Operational changes to the pump**, from strong magnets temporarily or permanently stopping the pump motor or electrical interference causing a pump memory error, resulting in loss of or change in therapy, which may lead to a return of underlying symptoms, drug withdrawal symptoms, or a clinically significant or fatal drug underdose. In the case of a pump memory error or a change to "safe state," reprogramming by a clinician is required.
- **Changes in flow rate**, from warming of the implanted pump, resulting in overinfusion and a clinically significant or fatal drug overdose.

Refer to Table 1 on page 14 and "Appendix: Electromagnetic interference" on page 22 for information on sources of EMI, the effect of EMI on the patient and the infusion system, and instructions on how to reduce the risk from EMI.

For information about the effects of EMI on programming, refer to "Telemetry signal disruption from EMI" on page 17.

 **Magnetic resonance imaging (MRI)**— The SynchroMed II infusion system has been found to be MR Conditional. MR scan eligibility is based on specific settings and conditions. Scanning under different conditions may result in a life-threatening injury or device malfunction.

Do not perform an MRI examination on a patient implanted with this device until you have read and understood the full MRI eligibility information in the MRI guidelines for Medtronic implantable infusion systems manual.

Table 1. Potential effects of EMI from devices or procedures

Device or procedure	Patient injury	System damage^a	Operational changes^a	Change in flow rate	For guidelines
Bone growth stimulators			X		page 22
Defibrillation/ cardioversion		X			page 22
Diathermy (including therapeutic ultrasound)	X			X	page 22
Electromagnetic field devices: (eg, arc welding, power stations)			X		page 22
Lithotripsy		X			page 23
Laser procedures				X	page 23
Magnetic resonance imaging (MRI)	X	X ^b	X	X	See MRI guidelines manual
Psychotherapeu tic procedures			X	X	page 23
Radiation therapy		X			page 23
Radio-frequency (RF)/ microwave ablation			X	X	page 23
Theft detector			X		page 23

^a Applies to SynchroMed II Pumps only.

^b Bench testing indicates that damage to SynchroMed II Pumps can occur; however, pump implantation requirements and patient orientation in a horizontal, closed-bore MRI system make this potential damage clinically unlikely. There has been no reported permanent damage to SynchroMed II Pumps due to clinical 1.5- or 3.0-Tesla (T) MRI exposure.

Precautions

Storage

Component packaging - Before shipment the components in the sterile package were sterilized by the process indicated on the package label. Do not use or implant a component if the following circumstances have occurred:

- The storage package or sterile seal has been pierced or altered because component sterility cannot be guaranteed and infection may occur.
- The component shows signs of damage because the component may not function properly.
- The use-by date has expired because component sterility cannot be guaranteed and infection may occur; also, device battery longevity may be reduced and may require early replacement.

Pump resterilization - Do not resterilize the pump. The pump is sterilized prior to shipment. Do not steam or flash autoclave the pump. At high temperatures, the pump can explode, resulting in equipment damage or personal injury.

Catheter resterilization - Do not resterilize the catheter because resterilization may damage the catheter.

Single use only - Do not reuse any component. Components are intended for single use only. Reusing components can result in inadequate therapy and an increased risk of infection.

Storage temperature: catheters - Do not store or transport the catheter and accessories above 57 °C (135 °F) or below -34 °C (-30 °F). Temperatures outside this range can damage components.

Storage temperature: kits and accessories - Do not store or transport the kit device components or accessories above 57 °C (135 °F) or below -34 °C (-30 °F). Temperatures outside this range can damage device components.

Transport temperature: pumps - Transport is <48 hours. Do not transport the pump above 55 °C (131 °F) or below 5 °C (40 °F). Temperatures outside this range can damage components.

Storage temperature: pumps - Storage is ≥ 48 hours. Do not store the pump above 30 °C (86 °F) or below 15 °C (59 °F). Temperatures outside this range can damage components.

System implant

Catheter access port kit components - Use the appropriate Medtronic catheter access port kit during all catheter access port procedures for Medtronic implantable infusion pumps. Using components other than Medtronic components or a kit other than the appropriate catheter access port kit can damage Medtronic components, requiring surgical revision or replacement, and allow drug leakage into surrounding tissue, resulting in tissue damage or loss of or change in therapy, which may lead to a return of underlying symptoms, drug withdrawal symptoms, or a clinically significant or fatal drug underdose.

Cerebrospinal fluid leak - For patients prone to cerebrospinal fluid (CSF) leaks, consider special procedures, such as a blood patch, to minimize the potential for CSF leaks. CSF leaks can cause seromas and severe spinal headaches.

Compatibility, all components - Follow these guidelines when selecting system components:

- **Medtronic components:** For proper therapy, use only components that are compatible with the appropriate indication.
- **Non-Medtronic components:** No claims of safety, efficacy, or compatibility are made with regard to the use of non-Medtronic components with Medtronic components. Refer to the non-Medtronic documentation for information.

Component handling - Handle the implantable components of this system with extreme care. These components may be damaged by excessive traction or sharp instruments, requiring surgical replacement. Refer to the appropriate implant manual for additional instructions.

Pump location - Select a location in the lower abdomen that is:

- away from bony structures (eg, 3 to 4 cm) to minimize discomfort at the pump site.
- away from areas of restriction or pressure to minimize the potential for skin erosion and patient discomfort.
- away from existing scar tissue.

For programmable pumps, select a location that is also:

- a minimum of 20 cm away from another programmable device to minimize telemetry interference and incorrect or incomplete programming.
- in an area accessible to the patient for proper operation of a patient control device (if applicable).

In the pediatric population, care must be taken to select an appropriate location by taking into consideration:

- available body mass.
- presence of ostomies.
- growth and development.

Refill kit components - Use the appropriate Medtronic refill kit during all refill procedures for Medtronic implantable infusion pumps. Using components other than Medtronic components or a kit other than the appropriate refill kit can damage Medtronic components, requiring surgical revision or replacement, and allow drug leakage into surrounding tissue, resulting in tissue damage or loss of or change in therapy, which may lead to a return of underlying symptoms, drug withdrawal symptoms, or a clinically significant or fatal drug underdose or overdose.

Replacement surgery - Patient management should be increased following pump or catheter replacement to ensure quick response to any signs of underdose or overdose.

Therapy discontinuance - If therapy is discontinued for an extended period, fill the pump reservoir with preservative-free saline. For programmable pumps, program the pump to minimum rate mode (0.006 mL/day). Refill the pump as needed to ensure the pump always contains fluid in the reservoir and fluid pathway. Stopping the pump for extended

periods or allowing the pump reservoir to empty completely can damage the system and require surgical replacement.

Clinician programming

Clinician programmer interaction with a cochlear implant - When the patient has a cochlear implant, minimize or eliminate the potential for unintended audible clicks during telemetry by keeping the external portion of the cochlear system as far from the programming components as possible or by turning off the cochlear implant during programming.

Clinician programmer interaction with flammable atmospheres - The programmer components are not certified for use in the presence of a flammable anaesthetic mixture with air or with oxygen or nitrous oxide. The consequences of using the programmer components near flammable atmospheres are unknown.

Clinician programmer interaction with other active implanted devices - When a patient has a programmable pump and another active implanted device (eg, pacemaker, defibrillator, neurostimulator):

- the radio-frequency (RF) signal used to program either device can reset or reprogram the other device.
- the magnet in a cardiac programmer may temporarily stop the pump.

To verify that inadvertent programming did not occur, clinicians familiar with each device should check the programmed parameters of each device before the patient is discharged from the hospital and after each programming session of either device (or as soon as possible after these times).

Also, inform patients to contact their physician immediately if they experience symptoms that could be related to either device or to the medical condition treated by either device.

Telemetry signal disruption from EMI - Do not attempt telemetry near equipment that may generate electromagnetic interference (EMI). EMI can interfere with programmer telemetry. If EMI disrupts programming, move the programmer away from the likely source of EMI. Examples of sources of EMI are magnetic resonance imaging (MRI), lithotripsy, computer monitors, cellular telephones, motorized wheelchairs, x-ray equipment, and other monitoring equipment. Interrupting telemetry can result in incorrect or incomplete programming.

Component disposal

When explanting a device (eg, replacement, cessation of therapy, or postmortem), or when disposing of accessories, follow these guidelines:

- If possible, return the explanted device with completed paperwork to Medtronic for analysis and disposal. See the back cover for the mailing addresses.
- To allow for device analysis, do not autoclave the device or expose the device to ultrasonic cleaners.
- Dispose of any unreturned components according to local environmental regulations; in some countries, explanting a battery-powered implantable device is mandatory.
 - Do not incinerate or cremate the device because it may explode if subjected to these temperatures.
 - Do not reuse any implantable device or implantable accessory after exposure to body tissues or fluids because the functionality of the component cannot be guaranteed.

Individualization of Treatment

Best results are achieved when the patient is fully informed about the therapy risks and benefits, surgical procedure, follow-up requirements, and self-care responsibilities. Maximum benefits from the infusion system require long-term postsurgical management. Medtronic implantable infusion systems are only approved for use with specific drugs. Follow the recommended doses in the drug labeling. The risk of inflammatory mass occurrence appears to be cumulative over time and increases with higher concentrations of opioids, therefore the lowest effective dose and concentration of opioids is recommended.

Adverse events summary

Adverse events summary - The implantation of an infusion system for intraspinal delivery involves risks that are similar to other spinal procedures. In addition to the risks associated with surgery, the following adverse events may occur with implantation or use of an infusion system:

- Pocket seroma, hematoma, erosion, or infection
- Infection
- Pump inversion (“flipping”)
- Pump movement and migration within the body
- Placement of the catheter may expose patients to risks of postlumbar puncture (spinal headache), CSF leak and CSF subcutaneous collection or rare central nervous system (CNS) pressure-related problems, radiculitis, arachnoiditis, bleeding, spinal cord damage, or meningitis
- Inflammatory mass could result in neurological impairment, including paralysis

- Allergic or immune system response to the implanted materials. A listing of device materials can be found in the Device Specifications sections of the implant manuals for the pump and catheters.

System-related complications

- End of device service life or component failure, requiring surgical replacement
- Component failure, resulting in loss of therapy, drug overdose, or inability to program the pump
- Catheter damage, dislodgement, migration, disconnection, kinking or occlusion, fibrosis, or hygroma, resulting in tissue damage or a loss of or change in therapy, and contributing to overinfusion or other potentially serious adverse health consequences.

Procedure-related complications

- Pump implanted upside down
- Improper handling of components before, during, or after implantation
- Reservoir contamination
- Improper injection through the catheter access port
- Injection into the pocket or subcutaneous tissue
- Activation of the reservoir valve (if present)
- Overpressurization of the reservoir, including by overfilling
- Programming error
- Tunneling during the catheter implant procedure may expose patients to risks of serious injury or death due to perforation of vital organs and/or major blood vessels.
- Detached catheter tip or catheter fragment(s) in the intrathecal space:
 - Residual catheter fragments may migrate, including rarely into the intracranial cavity, potentially resulting in serious adverse health consequences that may require surgical removal.
 - Residual catheter fragments in the CSF may compromise antibiotic effectiveness in the presence of a concomitant CSF infection.

Drug-related complications

- Local or systemic drug toxicity and related side effects
- Inflammatory mass formation at the tip of the implanted catheter particularly in patients who receive intraspinal morphine or other opioid drugs

Recognition of inflammatory mass

For patients receiving intrathecal opioids, the following **prodromal**, or **warning** signs or symptoms may occur before the onset of more severe neurological impairment:

- Change in the character, quality, or intensity of pain
- New radicular pain, especially at or near the dermatomal level of the catheter tip
- Frequent or large escalations of the daily drug dose are required to maintain the analgesic effect
- Dose escalations alleviate the increasing pain only temporarily

For patients receiving intrathecal baclofen as a sole agent, the following prodromal, or warning signs or symptoms may occur before the onset of more severe neurological impairment¹:

- Change in the character, quality, or intensity of spasticity
- Frequent or large escalations of the daily drug dose are required to maintain the antispastic effect
- Rapid dose escalations alleviate the increasing spasticity only temporarily

All patients on intraspinal opioid therapy should be monitored carefully at each visit for any new neurological signs or symptoms, including:

- New or different sensory symptoms (eg, numbness, tingling, burning, hyperesthesia, hyperalgesia)
- New, occasional, or intermittent bowel or bladder sphincter dysfunction
- New motor weakness, change in gait, or difficulty walking
- Any neurological symptom or sign that differs from baseline (eg, reflex changes)

In patients with new neurological signs or symptoms, consider neurosurgical consultation and the prompt performance of an imaging procedure (eg, MRI with and without intravenous contrast or CT myelogram) to confirm or rule out the diagnosis of an inflammatory mass.

Treatment of inflammatory mass

Timely treatment may minimize, or help to avert permanent neurological injury.

If an inflammatory mass is detected early in its clinical course, a decrease or discontinuation of opioid delivery into the mass may cause it to shrink or disappear without the need for surgical removal.

Note: Refer to the emergency procedures included in the refill kit manual for information on emptying the pump. Stopping the pump for more than a few days can cause the rotor to stall permanently. If therapy is to be discontinued for an extended period of time, the pump should be filled with preservative-free saline and programmed to minimum rate mode (0.006 mL/day).

Depending upon an individual patient's clinical condition, intraspinal therapy may be continued after one of the following interventions:

- Withdraw the catheter to a level below the inflammatory mass.
- Remove the involved catheter and replace it with a new catheter positioned below the inflammatory mass.
- Disconnect the involved catheter from the connector (two-piece catheter), or transect the involved catheter above the level of the lumbodorsal fascia (one-piece catheter) leaving the intraspinal catheter segment undisturbed. Ligate the exposed end of involved catheter to prevent CSF loss. Implant a new catheter with its tip below the inflammatory mass, and connect the new catheter to the proximal (pump) catheter segment. For more information about catheter ligation, contact Medtronic.

¹ Based on three case reports of patients from Murphy and Deer, respectively - Murphy PM, Skouvaklis DE, Amadeo RJJ et al. *Intrathecal Catheter Granuloma Associated with Isolated Baclofen Infusion*, *Anesthesia Analgesia* 2007; 102:848-852. Deer TR, Raso LJ, Garten TG. *Inflammatory Mass of an Intrathecal Catheter in Patients Receiving Baclofen as a Sole Agent: A Report of Two Cases and a Review of the Identification and Treatment of the Complication*. *Pain Medicine* 2007; 8(3):259-262.

Prompt open surgical removal of the mass or decompression of the spinal canal should be considered in patients who have a significant or progressive neurological deficit.

Mitigation of inflammatory mass

Intraspinal therapy should be administered to achieve adequate clinical response for as long as possible at the lowest effective dose and concentration.

For the treatment of pain patients, whenever medically possible, the tip of the intraspinal catheter should be placed in the lumbar thecal sac, below the conus medullaris. Lumbar placement may lessen the neurological consequences if an inflammatory mass develops.

Patients who receive intraspinal opioid therapy should be monitored carefully at each visit for any new clinical and neurological signs or symptoms.

Patient Counseling Information

Physicians should provide patients with information about:

- the components of the infusion system: catheter and pump.
- where the components are implanted in the body.
- instructions for using the infusion system.
- the indications, contraindications, warnings, and precautions for the infusion system.
- inflammatory mass and the related prodromal clinical symptoms.
- their therapy.

Physicians should also instruct patients to:

- always inform any health care personnel that they have an implanted infusion system before any procedure is begun.
- contact their physician if they notice any unusual symptoms or signs including:
 - signs and symptoms of drug overdose
 - signs and symptoms of drug underdose or withdrawal
- read the patient manual.
- avoid use of concomitant drugs without medical supervision.

Appendix: Electromagnetic interference

Please review "Electromagnetic interference" on page 13 and Table 1: "Potential effects of EMI from devices or procedures" on page 14.

Before any medical procedure is begun, patients should always inform any health care personnel that they have an implanted infusion system and share this information about EMI with them. The potential for the following effects results from an interaction of the infusion system and equipment—even when both are working properly.

Warnings

EMI from the following medical procedures or equipment may damage the device, interfere with device operation, or cause harm to the patient. If these procedures are required, follow the guidelines below:

Diathermy (including therapeutic ultrasound) - Avoid using shortwave (RF) diathermy within 30 cm (12 in) of the pump or catheter. Energy from diathermy can produce a significant increase in temperature in the area of the pump and continue to heat the tissue in a localized area because the pump can retain heat. If heated beyond 55 °C (131 °F), the pump can deliver more than the prescribed amount of drug, potentially causing a drug overdose. Therapeutic ultrasound is the use of ultrasound at higher energies than diagnostic ultrasound to bring heat or agitation into the body. Therapeutic ultrasound is acceptable if treatment is performed with a minimum separation of 15 cm (6 in) between the applicator and the implanted infusion system.

Magnetic Resonance Imaging - Refer to the MRI guidelines for Medtronic implantable infusions systems manual.

Precautions

EMI from the following equipment is unlikely to affect the infusion system if the guidelines below are followed:

Bone growth stimulators - Keep external magnetic field bone growth stimulator coils 45 cm away from the infusion system. After using either an implantable or external bone growth stimulator, ensure the infusion system is working as intended.

Defibrillation or cardioversion - When a patient is in ventricular or atrial fibrillation, the first consideration is patient survival. Testing indicates defibrillation is unlikely to damage the pump; however, after defibrillation, confirm the pump is functioning as intended.

Electromagnetic field devices - Testing indicates that the pump motor will stop while exposed to magnetic fields of 20 gauss or more. Less powerful magnets at closer distances may also stop the pump. Magnetic fields of 10 gauss or less will generally not affect the pump. Exercise care and avoid prolonged exposure to the following equipment or environments:

- Electric arc welding equipment
- High-voltage areas (safe if outside the fenced area)
- Microwave communication transmitters (safe if outside the fenced area)
- Television and radio transmitting towers (safe if outside the fenced area)

- Therapeutic magnets (eg, magnetic mattresses, blankets, wrist wraps, elbow wraps) greater than 20 gauss at the pump

If patients suspect that prolonged exposure to equipment is interfering with pump function, they should do the following:

1. Move away from the equipment or object.
2. If possible, turn off the equipment or object.
3. Inform the equipment owner or operator of the occurrence.

If the above actions do not resolve the effects of the interference, or the patients suspect that their therapy has been affected by exposure to EMI, they should contact their physician.

Lithotripsy - Safety has not been established. Lithotripsy may damage the pump or catheter and is not recommended for patients who have an implanted pump. If lithotripsy must be used, do not focus the beam on the pump or catheter and interrogate the pump following the procedure to check for alarms.

Laser procedures - Keep the laser directed away from the infusion system.

Psychotherapeutic procedures - Safety has not been established for psychotherapeutic procedures using equipment that generates electromagnetic interference (eg, electroconvulsive therapy, transcranial magnetic stimulation) in patients who have an implanted infusion system. Induced electrical currents may cause heating of the pump, resulting in overinfusion and a clinically significant or fatal drug overdose.

Radiation therapy - Exposing the pump to high doses of direct or scattered ionizing radiation from any source that results in an accumulated dose greater than 10 Gy may damage the device or cause it to reset to a non-therapeutic rate. To limit device exposure, use appropriate shielding or other measures wherever practicable. For patients who are undergoing multiple radiation treatments, consider the accumulated dose to the device from previous exposures. Medtronic recommends checking the pump with the clinician programmer after radiation exposure, if reversion to a non-therapeutic rate is a concern.

Radio-frequency or microwave ablation - Safety has not been established for radio-frequency (RF) or microwave ablation in patients who have an implanted infusion system. Induced electrical currents may cause heating of the pump, resulting in overinfusion and a clinically significant or fatal drug overdose.

Theft detectors and security screening devices - When patients approach theft detector and security screening devices (such as those found in airports, libraries, and some department stores), they should not linger near or lean on the security screening device.

Notes

Household items - Most household appliances and equipment, if working properly and grounded properly, will not interfere with the infusion system.

Other medical procedures - EMI from the following medical procedures is unlikely to affect the infusion system:

- Computerized axial tomography (CT or CAT) scans
- Diagnostic ultrasound (eg, carotid scan, doppler studies)

Note: To minimize potential image distortion, keep the transducer 15 cm away from the infusion system.

- Diagnostic x-rays or fluoroscopy
- Electrocautery
- Magnetoencephalography (MEG)
- Positron emission tomography (PET) scans

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2019-10-01
M961343A014 Rev A