Medtronic

IsoMed®

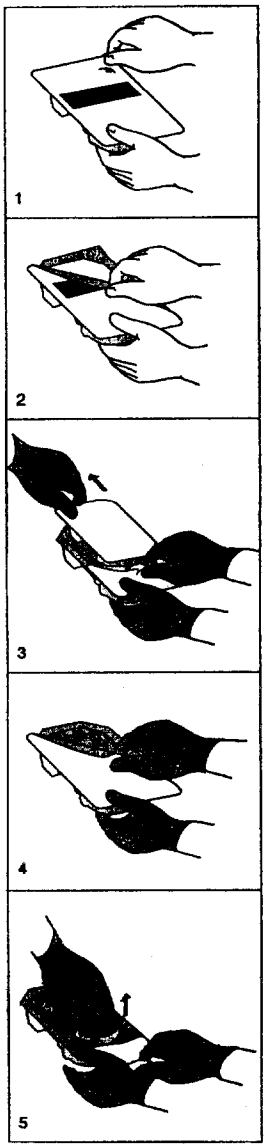
8472

Implantable Constant-Flow
Infusion Pump

Caution: Federal law restricts this device to sale by or on the order of a physician.

Technical Manual

Sterile Package Opening Instructions



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Introduction

The implantable Medtronic® IsoMed® Constant-Flow Infusion Pump (pump) is part of the IsoMed Constant-Flow Infusion System designed to contain and administer parenteral drugs to a specific site. The components of the IsoMed Constant Flow Infusion System include the pump, Medtronic catheter, catheter accessories, Medtronic refill kit, and Medtronic catheter access port kit. For a list of model numbers and components compatible with the pump, see the System Components Sheet packaged with this manual in the pump shelf box.

Do not implant, fill, refill, or access the catheter access port of an IsoMed pump without ensuring a thorough familiarity with the information contained in this technical manual. Failure to strictly adhere to these technical instructions can result in complications from a failure of the intended therapy to a clinically significant or fatal drug overdose.

Package Contents

- One IsoMed Model 8472 Constant-Flow Infusion Pump with suture loops
- Product literature

Introduction

Indications

The IsoMed® Constant-Flow Infusion System is indicated for use when patient therapy requires the chronic infusion of the drugs or fluids referred to in this manual.

The drugs or fluids approved for use with the IsoMed Constant-Flow Infusion System and their applications include the following:

- the chronic 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.
- the chronic intravascular infusion of floxuridine (FUDR) for the treatment of primary or metastatic cancer. Bacteriostatic water, or physiological saline 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 catheter patency.

Physicians prescribing the IsoMed Constant-Flow Infusion System for use with these drugs must be familiar with the drug stability information listed in "Drug Information".

Physicians prescribing the IsoMed Constant-Flow Infusion System for use with these drugs must be familiar with the indications, contraindications, warnings, precautions, adverse events, dosage and administration information, and screening procedures described in the drug labeling. **Except under approved conditions of investigational use, the use of IsoMed Constant-Flow Infusion System is restricted to the infusion of the drugs and fluids described in this manual.**

Contraindications

Implantation of this device is contraindicated in the presence of infection.

Implantation of this device is contraindicated when the pump cannot be implanted 1 inch (2.5 cm) or less from the surface of the skin.

Implantation of this device is contraindicated in patients whose body size is not sufficient to accept the pump bulk and weight.

Blood sampling through the catheter access port is contraindicated. The catheter access port has not been tested for blood withdrawal. If the presence of blood in the catheter access port is suspected, flush with a minimum of 10 ml saline (a heparinized solution may be used if not contraindicated).

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

Floxuridine should be used with added caution in patients with impaired hepatic or renal function.

Patients with known disease extending beyond an area capable of infusion should be considered for systemic therapy with other therapeutic agents.

Warnings

General

General Use — Improper use of implanted, constant flow infusion pumps could result in drug under- or overdose. Users must comply with product instructions for initial pump preparation, implantation, initial filling, refilling, and injecting into the catheter access port of the pump. Technical errors may result in a return of underlying symptoms, drug withdrawal symptoms, or a clinically significant or fatal drug overdose.

Drug Information/Labeling — Physicians prescribing the IsoMed Constant-Flow Infusion System must be familiar with the drug stability information listed in "Drug Information," and the indications, contraindications, warnings, and dosage and administration information described in the prescribed drug labeling.

Drug Removal — A significant amount of drug may be present in the pump reservoir, pump tubing, catheter access port, and catheter. Caution must be used to prevent drug overdose during injections through the catheter access port or when decreasing concentrations or changing solutions in the pump reservoir.

- To prevent drug overdose during injections through the catheter access port, aspirate approximately 1 - 2 ml from the catheter to ensure drug removal unless contraindicated (e.g., vascular applications). Refer to the appropriate catheter technical manual for specific catheter volume.
- To prevent drug overdose when decreasing concentrations or changing solutions in the pump reservoir, always rinse the reservoir twice between solutions to remove the drug that remains in the reservoir after emptying the pump. Refer to "Appendix B: Performing a Reservoir Rinse" for this procedure.

Infusion Solution Calculation — Correct calculation of the infusion solution is of critical importance in preventing over- or underinfusion. Refer to "Appendix A: Calculations" for instructions on calculating infusion solution.

Mixing Drugs — The effects of mixing drugs are unknown. Pump flow rate may decrease or stop if drug precipitation occurs.

Pump Overpressurization — Overpressurization of the pump reservoir can result in overinfusion, which can lead to a clinically significant or fatal drug overdose or cause damage to the pump.

Warnings

PreImplant

Pump Packaging — Carefully examine the shipping package and sterile tray (sterilization method: ethylene oxide gas). If the package is damaged, the sterile seal is broken, or the Use Before date is past, **do not implant or resterilize the pump**. Contact your Medtronic representative.

Single Use Only — The pump is intended for Single Use Only — **do not reuse.**

Patient Information — During presurgical discussions, give the patient complete information concerning adverse events, emergency procedures, system complications or system failure, initial fill, refill and catheter access port procedures, refill schedules, the consequences of "Twiddler's Syndrome" (manipulation of the pump through the skin), and the pump's weight and degree of protrusion.

Implant

Implanted Catheter Volume — During catheter placement, always calculate the implanted catheter length, determine the catheter volume, and record this information in the patient's medical record. The precise catheter model number, implanted catheter length, and pump flow rate are of critical importance in calculating the time required for drug to advance to the catheter tip and in preventing a drug overdose when injecting into the catheter access port.

Pump Replacement — During pump revisions, which require pump removal from the pocket and a fill procedure, always follow the instructions in this technical manual for emptying and initial filling of the pump prior to replacing the pump in the pocket.

Components — The use of non-Medtronic components with this system can result in damage to Medtronic components, less than adequate therapy, or increased risks to the patient.

Implant Depth — Implant the pump 1 inch (2.5 cm) or less from the surface of the skin. Implantation depth of more than 1 inch can inhibit septum access.

Implant Location — Before suturing, verify that, after implantation, the pump center reservoir fill port and catheter access port will be easy to palpate, that the catheter will not become twisted or contorted, and that the catheter is secured well away from the center reservoir fill port and catheter access port.

Warnings

Postimplant

Improper Injection — Improper injection through the catheter access port or into the pump pocket can result in a clinically significant or fatal drug overdose. Refer to "Appendix D: Emergency Procedures" in this manual or the drug labeling for specific drug overdose symptoms and methods of management. To prevent drug overdose when filling or refilling the pump, or when injecting into the catheter access port of the pump

- identify the pump model and reservoir volume;
- identify the location of the center reservoir fill port and the catheter access port;
- use the instructions and other accessories provided in the appropriate Medtronic refill kit and the appropriate Medtronic catheter access port kit (see the System Components Sheet packaged with this manual in the pump shelf box);
- use the 22-gauge refill needles provided in the appropriate Medtronic refill kit for accessing the center reservoir fill port, and the 24-gauge catheter access port needle provided in the appropriate Medtronic catheter access port kit for accessing the catheter access port (see the System Components Sheet packaged with this manual in the pump shelf box);
- use other medical procedures as appropriate to verify the location of the center reservoir fill port septum or the catheter access port septum during needle insertion; and
- refer to the appropriate drug labeling for indications, contraindications, warnings, precautions, adverse events, dosage and administration information, and screening procedures.

Contrast Media — When injecting contrast media into the intrathecal space, only use a contrast medium indicated for intrathecal administration. Failure to use an indicated contrast medium may result in adverse events including, but not limited to, extreme pain, cramps, seizures, and death.

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

Qualifications

Implantation — IsoMed® pumps must be implanted only by qualified physicians.

Preparation for Implant — Individuals trained in the operation and handling of the IsoMed Constant-Flow Infusion System must coordinate the preparation of the pump for implantation.

Pump Prescription — Physicians must understand the concentration, dose and rate relationships before prescribing the pump. Failure to understand these relationships can lead to drug under- or overdose.

Refill — The pump must be refilled on a prescribed schedule only by qualified personnel. All refills must be in compliance with the procedures described in the appropriate Medtronic refill kit technical instructions (see the System Components Sheet packaged with this manual in the pump shelf box).

Catheter Access Port Injection— The catheter access port must be accessed only by qualified personnel. All injections into the catheter access port must be in compliance with the procedures described in the appropriate Medtronic catheter access port kit technical instructions (see the System Components Sheet packaged with this manual in the pump shelf box).

Storage and Handling

Storage Temperature — Do not expose the pump to temperatures above 110 °F (43 °C) or below 41 °F (5 °C).

Damage — Do not implant a pump that has been dropped onto a hard surface or shows signs of damage.

Sterilization — Do not steam autoclave or flash autoclave the pump prior to implant or following explant. The pump will explode at high temperatures.

Disposal — Do not incinerate the pump. Explosion can result if the pump is subjected to incineration or cremation temperature. Return all explanted pumps to Medtronic for safe disposal.

Precautions

Preimplant

Physician Responsibility — The implanting physician is responsible for choosing the surgical procedure, the techniques, and the intended therapy for the patient.

Nonfiltered Access Ports — Screening for drug response with implanted nonfiltered access ports is not recommended. For those patients who must be screened with such devices because of their medical condition, extreme care should be exercised to ensure aseptic conditions are maintained.

Pump Preparation and Implant

Antibiotics — Consider use of peri- and postoperative antibiotics for pump implantation and any subsequent surgical procedures.

Pump Operation — Do not implant the pump unless pump operation has been confirmed. Refer to "Preliminary Procedures."

Catheter Connections — Make sure catheter placement and connections are secure. Failure to adequately connect, secure, and/or suture catheters can result in dislodgement, disconnection, cessation of therapy, or delivery of drug to the pocket or the subcutaneous tissue.

Reservoir Fill

Refill Kit — The appropriate Medtronic refill kit MUST be used during all refill procedures for IsoMed pumps. Do not use a refill kit for catheter access port procedures. Use only the appropriate Medtronic catheter access port kit for all catheter access port procedures. Always use the instructions and accessories provided in the appropriate Medtronic refill kit when emptying, filling, or refilling the pump reservoir (see the System Components Sheet packaged with this manual in the pump shelf box).

Needles — Always use the 22-gauge refill needles provided in the appropriate Medtronic refill kit for accessing the center reservoir fill port. Use of other needles may prolong the procedure or damage the septum.

Needle Damage — Use of excessive force when inserting the needle into the center reservoir fill port may damage the needle tip.

Connections — Firmly tighten all connections to prevent leaks.

Infection — If local or systemic infection is suspected, use extreme caution when emptying and/or refilling the pump reservoir.

Emptying Pump — Always empty the pump reservoir completely before filling with the prescribed drug. Use the 22-gauge refill needle and extension tubing set provided in the appropriate Medtronic refill kit for this procedure (see the System Components Sheet packaged with this manual in the pump shelf box). Filling a pump reservoir that has not been emptied completely may result in overpressurization.

Reservoir Contents — The 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.

Fill Volume — Do not exceed the reservoir volume when filling the pump. Overfilling the pump reservoir may result in overpressurization.

Catheter Access Port Injection

Catheter Access Port Kit — The appropriate Medtronic catheter access port kit MUST be used during all catheter access port procedures for IsoMed pumps. Do not use a catheter access port kit for refill procedures. Use only the appropriate Medtronic refill kit for refill procedures. Always use the instructions and accessories provided in the appropriate Medtronic catheter access port kit when injecting into the catheter access port (see the System Components Sheet packaged with this manual in the pump shelf box).

Needles — Always use a 24-gauge or smaller needle. A 24-gauge catheter access port needle is provided in the appropriate Medtronic catheter access port kit for accessing the catheter access port. Use of other needles may prolong the procedure or damage the septum.

Needle Damage — The catheter access port is designed to allow entry of a 24-gauge or smaller needle. Use of excessive force when inserting the needle into the catheter access port may damage the needle tip.

Connections — Firmly tighten all connections to prevent leaks.

Infection — If local or systemic infection is suspected, use extreme caution when injecting into the catheter access port.

Injection Rate — Do not exceed an injection rate of 5 ml per minute when injecting into the catheter access port.

Nonfiltered Access Port — Always use a filter when injecting into the catheter access port. The catheter access port does not contain a bacterial-retentive filter.

Precautions

Syringe Size — Do not overpressurize the catheter access port when injecting fluids. Small syringes can generate very high fluid pressure. Except when clearing a catheter occlusion for vascular applications, syringes smaller than 10 ml should not be used for catheter access port injections when catheter patency is questionable.

Injection Volume — Injection of more than 0.5 ml of fluid into the catheter access port under high pressure may cause catheter disconnection or catheter damage and subsequent fluid leakage.

Intrathecal Applications

Non-Therapy Periods — If therapy is discontinued for an extended period of time, the pump should be emptied of the drug and filled with preservative-free saline to maintain a patent fluid pathway. Refill as needed to ensure the pump always contains fluid in the reservoir and pathway.

Solution — Use only preservative-free solutions for intrathecal applications.

Contrast Media — Do not inject contrast media into the pump reservoir. This may impair pump operation.

Vascular Applications

Non-Therapy Periods — If therapy is discontinued for an extended period of time, the pump should be emptied of the drug and filled with saline (a heparinized solution may be used if not contraindicated) to maintain vascular catheter patency. Refill as needed to ensure the pump always contains fluid in the reservoir and pathway.

Vesicant/Cytotoxic Drugs at Implant — If the drug to be used is a vesicant or has the potential to cause local tissue damage, do not put the drug into the pump until after implantation. Fill the pump and catheter with saline (a heparinized solution may be used if not contraindicated) instead of the drug.

Anticoagulants — Physicians prescribing anticoagulant therapy to maintain vascular catheter patency must be familiar with the indications, contraindications, warnings, and dosage and administration information described in the drug labeling.

Catheter Flush — To maintain catheter patency in vascular applications, flush the catheter through the catheter access port after every use and/or a minimum of once per month if a non-heparinized solution is used in the pump reservoir.

Aspirating — Do not aspirate the catheter during vascular applications. If the presence of blood is suspected in the catheter access port or catheter, flush the catheter access port with a minimum of 10 ml saline (a heparinized solution may be used if not contraindicated).

Catheter Occlusions — Vascular catheter occlusions may inhibit drug delivery. Be familiar with the instructions in "Clearing a Catheter Occlusion."

Postimplant Clinician and Patient Information

It is imperative that clinicians and patients are aware of the following information:

CSF Leaks — Clinicians should consider special procedures, such as a blood patch to prevent and reduce cerebrospinal fluid (CSF) leaks for those patients who are prone to CSF leaks.

Infection — Clinicians suspecting infection evidenced by, but not limited to, erythema, drainage, hyperemia, fever, swelling, and localized pain should perform appropriate diagnostic procedures and intervention.

Diathermy/Therapeutic Hyperthermia — Clinicians should avoid using diathermy or therapeutic hyperthermia near the implanted pump. Heat from diathermy or therapeutic hyperthermia may cause overinfusion.

Therapeutic Hypothermia — Clinicians should avoid using therapeutic hypothermia near the implanted pump. Reduced body temperature from hypothermia may cause underinfusion.

Lithotripsy — Clinicians must avoid exposing the pump to lithotripsy. The effects of exposure to lithotripsy are unknown.

Implant Site — Clinicians and patients should attempt to keep the implant site clean, dry, and protected from external pressure or irritation.

System Problems — Clinicians should contact Medtronic to evaluate and manage suspected system problems.

Precautions

Inflammatory Mass — Clinicians and patients should be aware that, in rare instances, the development of an inflammatory mass at the tip of the implanted intrathecal catheter may occur and can result in progressive clinical signs, which bear monitoring. These signs include a progressive change in the character, quality, or intensity of pain; an increase in the level and degree of pain despite dose escalation; sensory changes (i.e., numbness, tingling, burning); hyperesthesia and/or hyperalgesia. Presentations that require immediate diagnosis include bowel and/or bladder dysfunction, myelopathy, conus syndrome, gait disturbances or difficulty ambulating, and paraparesis or paralysis.

If the presence of an inflammatory mass is suspected, recommended evaluation should include a review of the patient history and neurological evaluation, radiological diagnostic procedures (such as MRI with contrast), and an appropriate clinical consultation.

Aseptic Techniques — Clinicians must use strict aseptic technique during refill and catheter access port procedures.

Drug Information — Clinicians must notify patients of the appropriate warnings and precautions associated with the prescribed drug, including drug overdose and underdose signs and symptoms.

Identification Card — Patients must carry their Medtronic Patient Identification Cards at all times.

Pressure and Temperature Changes — Patients must consult with their physician before engaging in activities involving pressure or temperature changes (e.g., scuba diving, saunas, hot tubs, hyperbaric chambers, long-duration flights, nonpressurized aircraft, etc.). Pressure and temperature changes can cause the pump to temporarily under- or overdispense the drug.

Precautions

"Twiddler's Syndrome" — Patients must avoid "Twiddler's Syndrome" (manipulation of the pump through the skin), which can cause catheter disconnection, angulation, kinking, or dislodgement.

Physical Activities — Patients must avoid physical activities that may damage the implant site or device.

System Performance — Patients must return to the clinic or physicians offices at regular intervals to monitor system performance.

Personal Physicians — Patients must notify personal and consulting physicians that they have an implanted pump.

Unusual Symptoms — Patients must consult their physicians if they notice any unusual symptoms or signs.

Refill Scheduling — Patients must return for refills at the prescribed time. Be aware that at refill the pump should contain at least 2 ml of fluid. The flow rate of the pump decreases rapidly and stops as the volume in the pump reservoir decreases from 2 ml to 0 ml. This can result in the potential loss of therapeutic effect or drug withdrawal symptoms.

Travel Plans — Patients must notify their physicians about travel plans so pump refills can be arranged.

Magnetic Resonance Imaging (MRI) Information

Exposure of IsoMed® pumps to Magnetic Resonance Imaging (MRI) fields of 1.5 T (Tesla) has demonstrated no impact on pump performance and a limited effect on the quality of the diagnostic information.

Testing on the IsoMed pump has established the following with regard to MRI safety and diagnostic issues.

Implant Heating During MRI Scans

Specific Absorption Rate (SAR): Presence of the pump can potentially cause a two-fold increase of the local temperature rise in tissues near the pump. During a 20-minute pulse sequence in a 1.5 T (Tesla) GE Signa Scanner with a whole-body average SAR of 1 W/kg, a temperature rise of 1 degree Celsius in a static phantom was observed near the pump implanted in the "abdomen" of the phantom. The temperature rise in a static phantom represents a worst case for physiological temperature rise and the 20-minute scan time is representative of a typical imaging session. Implanting the pump in other locations may result in higher temperature rises in tissues near the pump.

In the unlikely event that the patient experiences uncomfortable warmth near the pump, the MRI scan should be stopped and the scan parameters adjusted to reduce the SAR to comfortable levels.

Peripheral Nerve Stimulation

Time-Varying Gradient Magnetic Fields: Presence of the pump may potentially cause a two-fold increase of the induced electric field in tissues near the pump. With the pump implanted in the abdomen, using pulse sequences that have dB/dt up to 20 T/s, the measured induced electric field near the pump is below the threshold necessary to cause stimulation.

In the unlikely event that the patient reports stimulation during the scan, the proper procedure is the same as for patients without implants—stop the MRI scan and adjust the scan parameters to reduce the potential for nerve stimulation.

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Static Magnetic Field

For magnetic fields up to 1.5 T, the magnetic force and torque on the IsoMed pump will be less than the force and torque due to gravity.

In the unlikely event that the patient reports a slight tugging sensation at the pump implant site, an elastic garment or wrap may be used to prevent the pump from moving and reduce the sensation the patient may experience.

Image Distortion

The IsoMed pump will cause image dropout on MRI images in the region surrounding the pump. The extent of image artifact depends on the pulse sequence chosen with gradient echo sequences generally causing the most image dropout. Spin echo sequences will cause image dropout in a region approximately 50% larger than the pump itself, about 12 cm across, but with little image distortion or artifact beyond that region.

Minimizing Image Distortion

MR image artifact may be minimized by careful choice of pulse sequence parameters and location of the angle and location of the imaging plane. However, the reduction in image distortion obtained by adjustment of pulse sequence parameters will usually be at a cost in signal-to-noise ratio. These general principles should be followed:

- use imaging sequences with stronger gradients for both slice and read encoding directions. Employ higher bandwidth for both RF pulse and data sampling.
- choose an orientation for read-out axis that minimizes the appearance of in-plane distortion.
- use spin echo (SE) or gradient echo (GE) MR imaging sequences with a relatively high data sampling bandwidth.
- use shorter echo time (TE) for gradient echo technique, whenever possible.
- be aware that the actual imaging slice shape can be curved in space due to the presence of the field disturbance of the pump (as stated above).
- identify the location of the implant in the patient and when possible, orient all imaging slices away from the implanted pump.

Drug Information

Testing has indicated that the following drugs are stable and compatible with the IsoMed® Constant-Flow Infusion System. Refer to appropriate drug labeling for complete prescribing information, including indications, contraindications, warnings, precautions, and adverse events.

Note: When filling the pump reservoir, verify that the Use Before date of the drug will not occur before the patient returns for the next refill.

Table 1. Stability for Drugs Approved for Use with IsoMed® Constant-Flow Infusion System.

Drug	Stability
Morphine sulfate (preservative-free)	90 Days
Floxuridine (FUDR)	27 Days

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Observed Adverse Events

Clinical study of the IsoMed Constant-Flow Infusion System included 110 patients with chronic, intractable pain enrolled for intrathecal administration of analgesics, and 79 patients with primary or metastatic cancer enrolled for intravascular administration of chemotherapy. The average length of follow-up was 5.2 months (range of 0.0 to 14.5 months), with a cumulative experience of 984 months.

No unanticipated device-related adverse effects were reported during the studies. There were a total of 11 deaths in the studies; all were reported as due to disease progression or disease-related complications. Twelve pumps were explanted in the 189 patients studied.

Intrathecal Study

The intrathecal study involved 110 patients with chronic, intractable pain with a cumulative experience of 705.8 months. Tables 2 and 3 report the adverse events attributed to the investigational system (IsoMed pump and accessories), and the implant, explant, refill, and catheter access port procedures. All system-related adverse events that occurred in the study are included in the tables. The procedure-related adverse events that occurred more than once are included in the tables. The procedure-related adverse events that occurred only once are listed following each table.

Adverse Events

Table 2. Serious[a] Adverse Events (N = 110 patients)

Category / Adverse Event	Number of Events	Events per Patient Year	Number of Patients	Percent of Patients
SYSTEM-RELATED				
Unable to withdraw /inject into catheter access port	1	0.02	1	0.9%
PROCEDURE-RELATED[b]				
Implant				
Pocket hematoma/seroma	27	0.46	24	21.8%
CSF leak/accumulation	6	0.10	6	5.5%
Catheter cut/kink/dislodgement	4	0.07	4	3.6%
Pocket skin erosion/ wound dehiscence	4	0.07	4	3.6%
Pocket inflammation/ infection	3	0.05	3	2.7%
Explant				
CSF leak	2	0.03	2	1.8%

[a] Events that resulted in invasive intervention, death/disability, or hospitalization/prolonged hospitalization.

[b] Procedure-related ADE's with 2 or more occurrences observed in the study. Events that occurred only once are listed following the table.

Single Procedure-Related Serious Adverse Events — Each of the following procedure-related serious adverse events were observed only once in the study: aseptic meningitis, incisional pain, local trauma to nerve root, oversedation/severe post-op pain, lack of drug effect, pump impinging on rib, seroma/CSF hygroma, and pocket hematoma/seroma following explant.

Adverse Events

Table 3. Non-Serious Adverse Events (N = 110 patients)

Category / Adverse Event	Number of Events	Events per Patient Year	Number of Patients	Percent of Patients
SYSTEM-RELATED				
Dull needle in refill kit	1	0.02	1	0.9%
PROCEDURE-RELATED[a]				
Post-surgical pain/discomfort	15	0.25	15	13.6%
CSF leak	3	0.05	3	2.7%
Pocket inflammation	3	0.05	3	2.7%
Lumbar infection/inflammation	3	0.05	3	2.7%
Fill/refill error	2	0.03	2	1.8%

[a] Procedure-related ADE's with 2 or more occurrences observed in the study. Events that occurred only once are listed following the table.

Single Procedure-Related Non-Serious Adverse Events — Each of the following procedure-related non-serious adverse events were observed only once in the study: migration, pump pocket hematoma/seroma, persistent headache, post-op temperature, dull needle in refill kit, small defect at incision, upper respiratory infection, and increased leg pain.

Adverse Events

Intravascular Study

The intravascular study involved 79 patients with primary or metastatic cancer with a cumulative experience of 279 months. Tables 4 and 5 report the adverse events attributed to the investigational system (IsoMed pump and accessories), and the implant, explant, refill, and catheter access port procedures. All system-related adverse events that occurred in the study are included in the tables. The procedure-related adverse events that occurred more than once are included in the tables. The procedure-related adverse events that occurred only once are listed following each table.

Table 4. Serious[a] Adverse Events (N = 79 patients)

Category / Adverse Event	Number of Events	Events per Patient Year	Number of Patients	Percent of Patients
SYSTEM-RELATED				
Pump inversion	1	0.04	1	1.3%
PROCEDURE-RELATED[b]				
Pump pocket hematoma/seroma	9	0.34	8	10.1%
Pump pocket infection	5	0.21	5	6.3%

[a] Events that resulted in invasive intervention, death/disability, or hospitalization/prolonged hospitalization.

[b] Procedure-related ADE's with 2 or more occurrences observed in the study. Events that occurred only once are listed following the table.

Single Procedure-Related Serious Adverse Events — Each of the following procedure-related serious adverse events were observed only once in the study: underinfusion, pump migration, pump inversion, inability to withdraw from or inject into catheter access port, perforated small bowel, collapsed lung post-op, midline incision infection, elevated bilirubin, pancreatitis, and GI bleeding.

Table 5. Non-Serious Adverse Event Summary (N = 79 patients)

Category / Adverse Event	Number of Events	Events per Patient Year	Number of Patients	Percent of Patients
SYSTEM-RELATED				
Difficulty accessing/ entering reservoir	4	0.17	4	5.1%
Difficulty/pain during procedure	2	0.09	2	2.5%
Overinfusion	2	0.09	2	2.5%
Pump pocket pain	1	0.04	1	1.3%
Needle leak during refill	1	0.04	1	1.3%
Subcutaneous needle break	1	0.04	1	1.3%
Leakage at needle tubing junction (catheter access port kit)	1	0.04	1	1.3%
PROCEDURE-RELATED[a]				
Post surgical pain	4	0.17	4	5.1%
Pump pocket hematoma/seroma	3	0.13	3	3.8%
Pump pocket infection/inflammation	3	0.13	3	3.8%
Fever	3	0.13	3	3.8%
Migration/inversion	2	0.09	2	2.5%
Increased bilirubin	2	0.09	2	2.5%
Constipation	2	0.09	2	2.5%

[a] Procedure-related ADE's with 2 or more occurrences observed in the study. Events that occurred only once are listed following the table.

Single Procedure-Related Non-Serious Adverse Events — Each of the following procedure-related non-serious adverse events were observed only once in the study: unable to enter catheter access port, elevated temperature, urinary retention, edema (RLQ), incision drainage, hypotension, and colored residual fluid.

Adverse Events

Potential Adverse Events

The adverse events associated with the use of this device may include, but may not be limited to, the events that follow.

Pump Complications

Cessation of therapy, due to random component failure, which may result in

- return of underlying symptoms,
- drug withdrawal symptoms, or
- need for surgical removal of pump.

Change in flow performance characteristics, due to component failure, prolonged exposures to temperatures or pressures outside of normal exposures, or changes over time, which may result in

- underinfusion of drug,
- return of underlying symptoms,
- drug withdrawal symptoms,
- overinfusion of drug,
- drug overdose, or
- need for surgical removal of pump.

Catheter Complications

Change in catheter performance, due to catheter kinking, catheter disconnection, catheter leakage, catheter breakage, complete or partial catheter occlusion, catheter dislodgement or migration, or catheter fibrosis or hygroma, which may result in

- delivery of drug into pocket or subcutaneous tissue,
- drug withdrawal symptoms,
- return of underlying symptoms,
- free-floating catheter in the cerebrospinal fluid (CSF),
- underinfusion of drug,
- CSF leak leading to spinal headache, CSF subcutaneous collection, or CNS pressure-related problems,
- damage to the spinal cord,
- hemorrhage,
- need for surgical replacement/revision of catheter,

- organ failure,
- stroke, or
- death.

Drug Complications

- Local and systemic drug toxicity and related side effects
- Complications due to using drugs not in accordance with the drug labeling
- Complications due to use of unapproved drugs with the system
- Extravasation

Procedural Complications

Surgical

- Pump implanted upside down
- Pocket seroma, hematoma, erosion, or infection
- CSF leak leading to spinal headache, CSF subcutaneous collection, or rare CNS pressure-related problems
- Radiculitis
- Arachnoiditis
- Bleeding
- Damage to the spinal cord
- Meningitis
- Spinal headache
- Medical complications
- Complications from anesthesia
- Damage to the pump, catheter, and catheter access system due to improper handling and filling before, during, or after implantation
- Infection
- Arterial thrombosis
- Hemorrhage and exsanguination
- Stroke
- Organ failure
- Death

Adverse Events

Fill/Refill/Catheter Access Port Injection

- Infection
- Meningitis (intrathecal applications)
- Fill, refill, catheter access port injection error, which may lead to tissue damage or a clinically significant or fatal drug under- or overdose, or drug withdrawal
- Reservoir contamination
- Overpressurization of the reservoir, which can lead to a clinically significant or fatal drug overdose or damage to the pump
- Improper injection through the catheter access port, which can lead to a clinically significant or fatal drug overdose
- Injection into pocket or subcutaneous tissue

Other

- Body rejection phenomena
- Complications due to the interaction of the Medtronic neurological implantable pumps with unusual physiological variations in patients
- Surgical replacement of the pump or catheter due to any of the complications
- Complications due to other intervening acts

Clinical Studies

Two multi-center, prospective open-label clinical studies of the Medtronic® IsoMed® Constant-Flow Infusion System were conducted in the United States. The clinical studies were designed to demonstrate that the IsoMed pump accurately and safely delivers medications via intrathecal and intravascular routes of administration.

Study Overview

The primary objective of the clinical studies was to demonstrate that the IsoMed pump effectively (accurately) delivers medications to the intended (intrathecal and intravascular) site(s). The accuracy endpoint was the average clinically measured flow rate accuracy ratio, defined as the ratio of the measured volume delivered to the expected volume delivered at pump refill:

$$\textbf{Clinically measured flow rate accuracy ratio} = \frac{\textbf{Measured volume delivered}}{\textbf{Expected volume delivered}}$$

When the ratio is multiplied by 100, the result is the percent of the expected volume that was measured to have been delivered, equivalent to the flow rate accuracy.

The secondary objective of the clinical studies was to demonstrate that the IsoMed pump safely delivers medications to the intended site(s) based on the serious adverse events associated with the investigational system. Events that resulted in an invasive intervention, death/disability, or hospitalization/prolonged hospitalization were categorized as serious events.

The same statistical analysis methods were employed in both protocols for the same end points (i.e., accuracy and serious adverse events), which allowed the data from both studies to be "pooled" to demonstrate the performance of the device based on the combined data sets.

Intrathecal Study

The study was a non-randomized, prospective study of 110 patients enrolled at 11 U.S. sites. Patients received intrathecal administration of analgesics for chronic, intractable pain. The average length of follow-up was 6.4 months (range of 0.1 to 14.5 months), with a cumulative experience of 704.8 months.

Clinical Studies

Patients Studied

The patients, 58 female and 52 male, had an average age of 51 years (range of 26 to 88 years). One hundred and three (103) were enrolled with non-cancer pain, 7 had pain related to cancer or cancer-related treatment.

Methods

The primary objective of the study was to confirm that the average accuracy of the clinically measured flow rate (90% confidence limits) was within ±15% of the labeled flow rates. The patients had an average of 5.5 pump refills (range of 0 to 22 refills) with a total of 609 refills, 541 of which provided evaluable data.

The secondary objective was to demonstrate that the cumulative investigational system-related serious adverse event-free survival at 3 months was greater than 85% (lower confidence limit).

Results

The intrathecal study results are summarized in Table 6. The 106 patients with a total of 541 evaluable pump refills demonstrated an average clinically measured flow rate accuracy of 99% (90% confidence interval of 96–100%). The serious adverse event-free survival at 3 months (related to the investigational system) was 100% (estimated 90% confidence interval of 96–100%).

Table 6. Intrathecal Study Results

Measure	Results	Experience	Number of Patients
Average clinically measured flow rate accuracy	99%	541 pump refills	106
Serious adverse event-free survival at 3 months[a]	100%	289.7 months	110

[a] Related to IsoMed pump and accessories.

Intravascular Study

The study was a non-randomized, prospective study of 79 patients enrolled at 13 U.S. sites. Patients received intrahepatic arterial administration of chemotherapy for the treatment of primary or metastatic liver cancer. The average length of follow-up was 3.5 months (range of 0.0 to 12.0 months), with a cumulative experience of 279.5 months.

Patients Studied

The patients, 49 male and 30 female, had an average age of 58 years (range of 23 to 83 years). Seventy five (75) were enrolled with colorectal cancer metastatic to the liver, 4 had other metastatic cancer.

Methods

The primary objective of the study was to confirm that the average accuracy of the clinically measured flow rate (90% confidence limits) was within ±15% of the labeled flow rates. The patients had an average of 6.2 pump refills (range of 0 to 25 refills) with a total of 487 refills, 419 of which provided evaluable data.

The secondary objective was to demonstrate that the cumulative investigational system-related serious adverse event-free survival was greater than 85% (lower confidence interval).

Results

The intravascular study results are summarized in Table 7. The 67 patients with a total of 419 evaluable pump refills demonstrated an average clinically measured flow rate accuracy of 91% (90% confidence interval of 88–91%). When adjusted for the effects of the drug viscosity and arterial pressure (factor of 0.9026 based on the offset of the mean flow rates of the intrathecal and intravascular data) the average clinically measured flow rate accuracy is 101% (90% confidence interval of 98–101%). The serious adverse event-free survival at 3 months (related to the investigational system) was 100% (estimated confidence interval of 93–100%).

Table 7. Intravascular Study Results

Measure	Results	Experience	Number of Patients
Average clinically measured flow rate accuracy	91%	419 pump refills	67
Average clinically measured flow rate accuracy adjusted for drug viscosity/arterial pressure	101%	419 pump refills	67
Serious adverse event-free survival at 3 months[a]	100%	169.4 months	79

[a] Related to IsoMed pump and accessories.

Pooled Study

Pooling of the study data resulted in a total of 189 patients enrolled at 24 U.S. sites. The average length of follow-up for the pooled data was 5.2 months (range of 0.0 to 14.5 months), with a cumulative experience of 984.3 months.

Patients Studied

The patients, 101 male and 88 female, had an average age of 51 years (range of 26 to 88 years). Table 8 provides a list of the pump models included in the studies.

Table 8. Pump Models Included in Clinical Studies

	Intrathecal Study		Intravascular Study		Combined	
Pump Model	N	(%)	N	(%)	N	(%)
8472-20-05	22	20.0%	--	--	22	11.6%
8472-20-10	--	--	4	5.1%	4	2.1%
8472-35-05	67	60.9%	--	--	67	35.4%
8472-35-10	9	8.2%	6	7.6%	15	7.9%
8472-35-15	1	0.9%	47	59.5%	48	25.4%
8472-60-15	11	10.0%	--	--	11	5.8%
8472-60-40	--	--	22	27.8%	22	11.6%
TOTAL	110	100.0%	79	100.0%	189	100.0%

Methods

Since the endpoints and analysis methods were the same for both studies, the data were pooled to provide results based on the combined experience. The flow rate accuracy data from the intrathecal and intravascular studies were pooled using the adjusted intravascular data set (0.9026 adjustment factor). The safety data was also pooled since pump implant technique and location, as well as clinician interaction, were essentially the same for both studies.

Results

The pooled study results are summarized in Table 9. The pooled data demonstrated an average clinically measured flow rate accuracy of 100% (90% confidence interval of 97–100%). The serious adverse event-free survival at 3 months (related to the investigational system) was 100% (estimated confidence interval of 98–100%).

Table 9. Pooled Study Results

Measure	Results	Experience	Number of Patients
Average clinically measured flow rate accuracy	100%	960 pump refills	173
Serious adverse event-free survival at 3 months[a]	100%	459.1 months	189

[a] Related to IsoMed pump and accessories.

With the exception of slightly elevated flow rates during the initial pump cycles, the average flow rates remained constant over time (based on the average flow rate accuracy ratios for pooled data by refill number using adjusted intravascular data and a minimum of 4 refills. Refer to Figure 1.

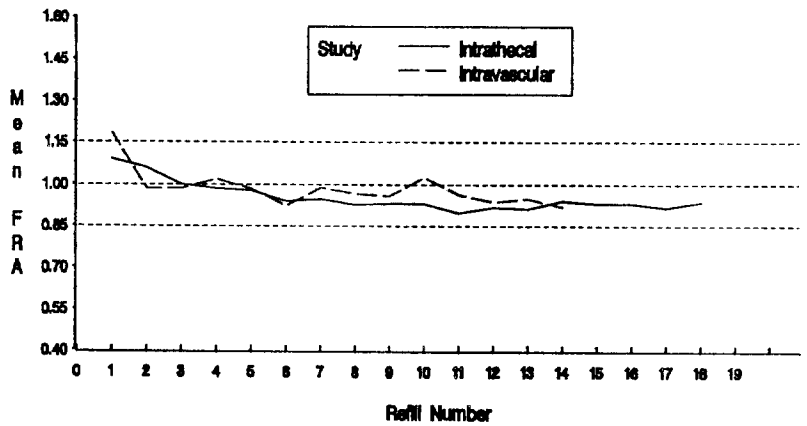
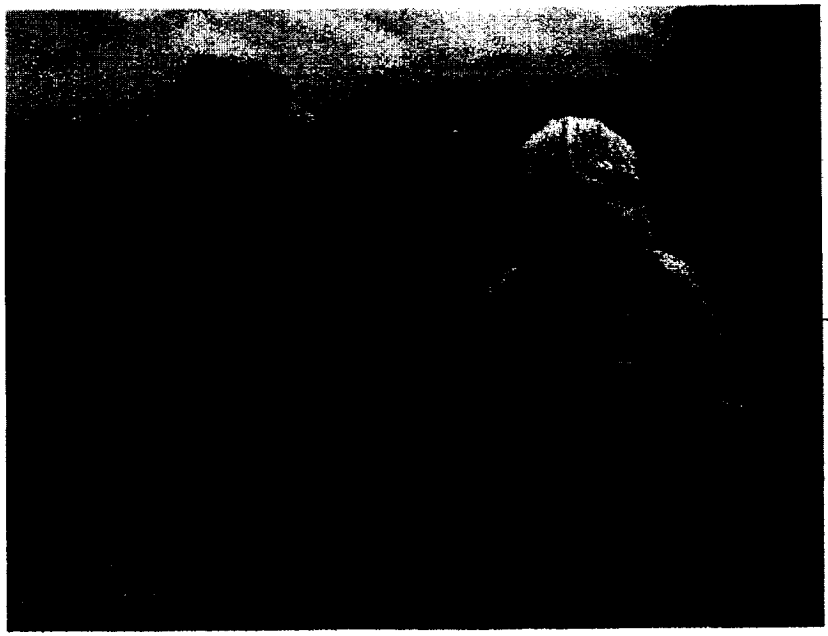


Figure 1. Average flow rate accuracy ratios by refill number.

Medtronic

IsoMed®

Constant-Flow Infusion System



Patient Information

Caution: Federal law restricts this device to sale by or on the order of a physician.

Contents

Introduction

Since Medtronic's founding in 1949, the company's goal has been to develop and produce medical devices that maintain or improve quality of life by restoring health.

This booklet will help you to learn about the IsoMed Constant-Flow Infusion System and how it works. Your family and friends will also find answers to many of their questions in the booklet.

This booklet describes the following:

- What the system does
- How the system works
- How the system is surgically placed
- How the system is refilled
- What you need to do
- How the system may affect you and your family

Important terms will appear in **bold** text and are listed in an alphabetized glossary at the end of this booklet. There is space at the end of this booklet for important names and telephone numbers.

You should discuss any questions you may have about the infusion system with your doctor or nurse. You may want to write questions or notes in the space provided at the end of this booklet.

What is the IsoMed® Constant-Flow Infusion System?

The IsoMed Constant-Flow Infusion System consists of a **pump** and **catheter**. They are placed in your body during a surgical procedure.

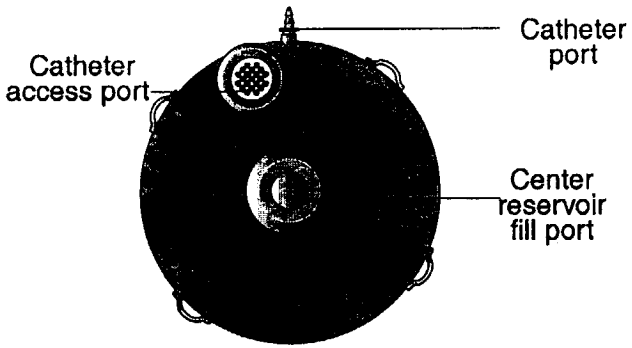
The **pump** is a round metal disk from 1 to 1.5 inches thick, 3 inches wide, and weighing about 4 ounces. It is made of titanium. The pump stores and releases prescribed amounts of medication through the catheter into your body. The pump has three main components: a **reservoir**, a **reservoir fill port**, and a **catheter access port**.

The **reservoir** is the space inside the pump that holds the medication. The pump's **reservoir size** is the amount of medication the pump can hold. The pump **flow rate** is the amount of medication the pump delivers over a specific time. The pump has a constant flow rate that was set during manufacturing. The **pump drive**, located behind the reservoir, is a gas that develops a specific pressure at body temperature and places a constant pressure on the reservoir to force the drug out.

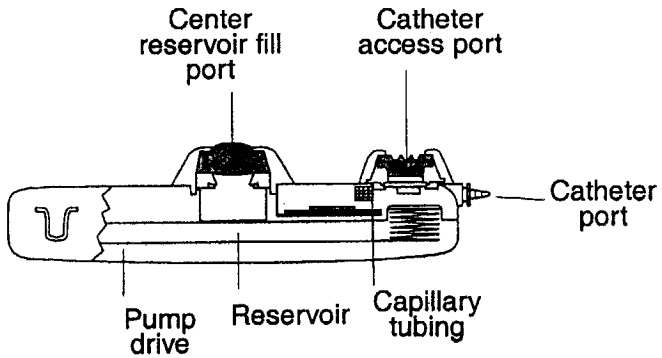
In the center of the pump is a **reservoir fill port**. To refill your pump, your doctor or nurse inserts a needle through your skin and through the silicone rubber **septum** in this port.

Near the edge of the pump is a **catheter access port**. The catheter access port allows your doctor or nurse to inject medications or solutions directly into the catheter.

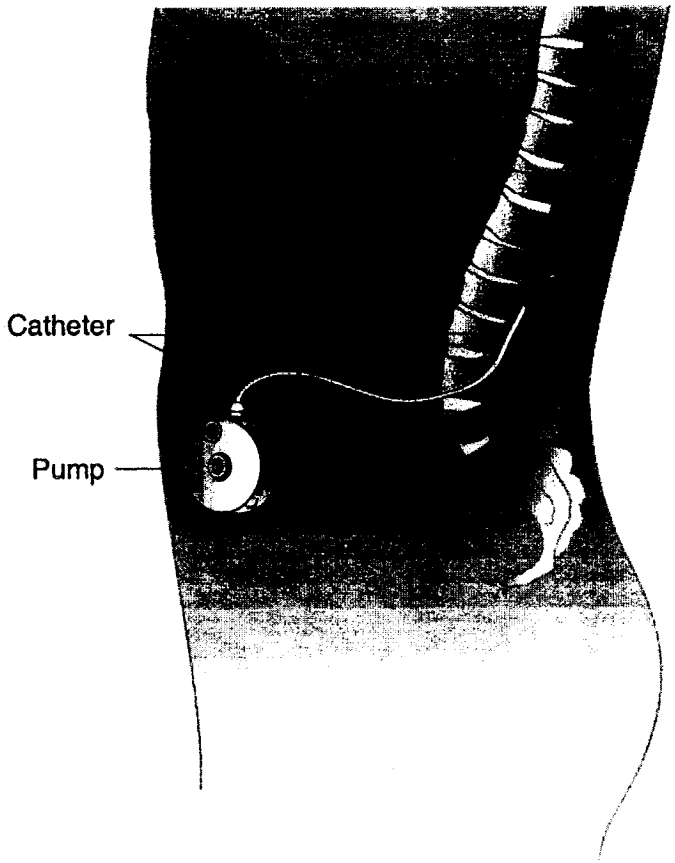
The **catheter** is a small, flexible tube made of silicone rubber that connects to the pump at the catheter port. The pump delivers medication through the catheter to the location in your body where it is likely to be most effective.



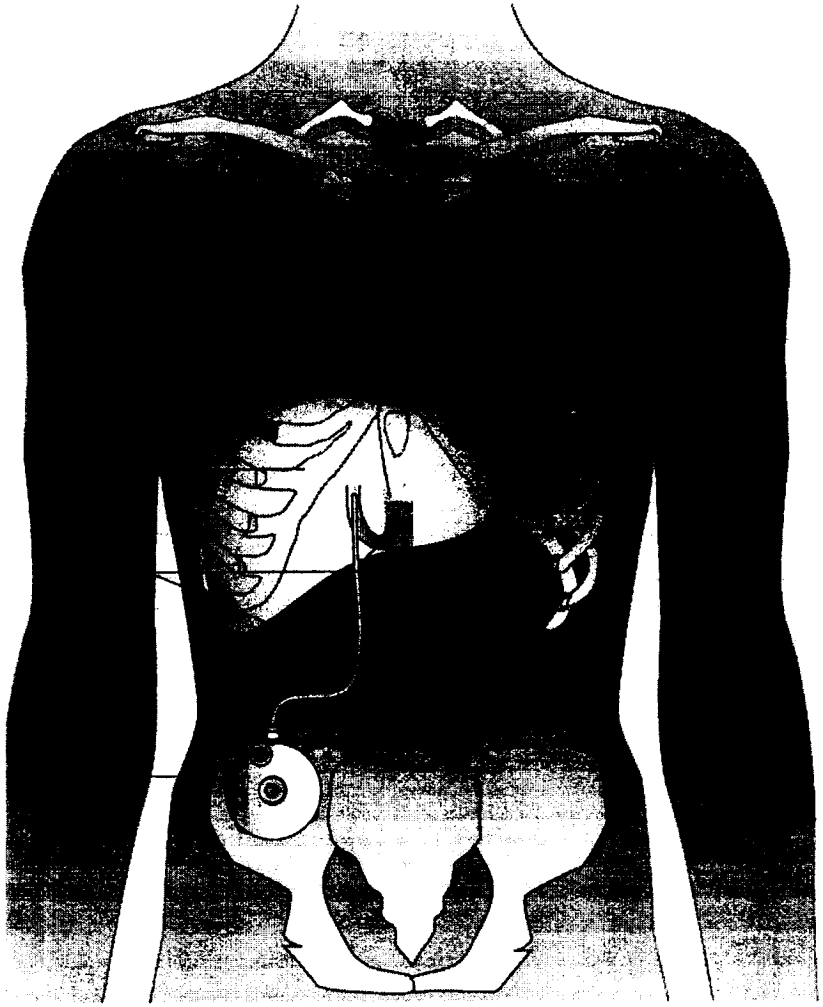
Top view of IsoMed Constant-Flow Infusion Pump.



Cutaway view of IsoMed Constant-Flow Infusion Pump.



Intrathecal drug delivery.



Arterial drug delivery.

Why an Infusion System?

An infusion system delivers medication directly to target sites within the body.

Infusion systems are typically used when more traditional therapies are considered ineffective or inappropriate. In the case of chronic pain, infusion systems are commonly used when oral, intravenous, or topical medications fail to provide enough pain relief or cause uncomfortable side effects. For chemotherapy, infusion systems are commonly used when non-direct delivery of medication (delivery not directed to a specific site or organ) is less effective or causes uncomfortable side effects.

Infusion systems are also used when alternative therapies such as an external pump with a catheter through the skin, or injections directly into the spine or internal organ are not effective enough or are uncomfortable for the patient.

Infusion systems are not recommended when infection or wide-spread disease is present, or when patient body size or weight is too small to accommodate the size of the pump.

Your doctor will tell you why this infusion system has been recommended for you. Your doctor will discuss with you any questions you may have about your therapy or how the system works.

Be sure to ask your doctor or nurse if there are areas of concern or things that you do not understand.

How Does My Infusion System Work?

The IsoMed Constant-Flow Infusion System is designed to continuously deliver medication through a catheter directly to the location in your body where it is likely to be most effective.

How Will My Infusion System Be Surgically Placed?

Your doctor will place the pump just under the skin of your abdomen. He or she will also place the catheter to deliver the medication from the pump to the proper location. Once the catheter and pump are in place, your doctor will attach the catheter to the pump.

How Will My Infusion System Be Refilled?

You will need to return to your doctor's office or clinic regularly to have your pump refilled. **Your pump must be refilled before it is completely empty.** As your pump nears empty, the flow rate decreases until it stops altogether. If the flow rate gets too low, or if the pump stops, you will not receive the prescribed amount of medication. This can result in a disruption in therapy or drug withdrawal symptoms.

Your return visits may vary from once a week to once every two to three months. This will depend on the flow rate and reservoir size of your pump, and on the medication and dosage your doctor recommends for you. Your pump is designed to last for many years and may be refilled as many times as necessary for your therapy.

During a typical refill visit, you will receive an injection to refill your pump. Your doctor will tell you what medication you are receiving and what possible side effects can occur. Your doctor will make sure you are receiving adequate therapy and discuss any questions you may have.

Potential Risks

Talk with your doctor about the risks associated with this therapy. Some examples are:

- Conditions resulting from the surgery, such as infections.
- Medication side effects.
- A disruption in your therapy if the pump and catheters are damaged, such as by improper handling or filling; by drugs or uses not intended for the pump; or by manipulating the pump or catheter through the skin. (Manipulation can result in moving the catheter or pump from its intended site, or plugging or tearing the catheter.)
- Overdose or underdose of medication if the pump is damaged by impact to the body in the area of the pump, as in strenuous exercise or contact sports.

- Overdose or underdose of medication if certain conditions affect the flow rate of the pump. Examples include:

  Patients who live at high altitudes, climb mountains, or travel in non-pressurized aircraft will be exposed to lower air pressure and might receive more medication than prescribed.

  Patients who scuba dive or undergo hyperbaric chamber treatment will be exposed to higher air pressure and might receive less medication than prescribed.

  Patients who have a fever might receive more medication than prescribed.

  Patients who have an increased body temperature from being exposed to high heat (as in diathermy treatments, saunas, or steam baths) might receive more medication than prescribed.

Talk to your doctor about the potential risks, related conditions, and benefits from this therapy before agreeing to treatment. Ask your doctor or nurse if there are areas of concern or things you feel you don't understand.

Living with Your Infusion System

Recovering from Surgery

After surgery there may be some pain at the location of your incision. After a few weeks, this discomfort should go away. Also with time, you should become used to the feeling of the pump inside your body.

Follow your doctor's advice about resuming your daily activities: work, bathing, recreation, hobbies, and exercise. Your doctor and the medical staff know your medical condition and are your best sources of advice.

When to Call Your Doctor

If any of the following events occur, contact your doctor.

- You develop a severe headache.
- You notice any swelling, redness, or pain near the location of your pump.
- You have a fever.
- You notice any numbness, tingling or burning, or any unusual sensitivity to pain, heat, cold or touch.
- You have any medication-related side effects or withdrawal symptoms.
- You feel you are not receiving adequate therapy.
- You feel that the symptoms you had before receiving your pump have returned.

What You Need to Do

The infusion system delivers medication automatically. However, you still need to take good care of yourself. Follow the advice your doctor gives you. Ask your doctor or nurse about anything you don't understand or any questions you may have.

- Carry your Patient Identification Card with you at all times.
- Tell your family doctor and dentist that you have an infusion system so they will be aware of this during any medical treatment.
- Keep all doctor appointments during your treatment.
- Follow your doctor's instructions about your activities after surgery.
- Avoid manipulating the pump through your skin.
- Avoid physical activities such as strenuous exercise or contact sports that may damage the surgical site, the pump, or the catheter.

- Avoid activities that may greatly affect the temperature or pressure of the pump without talking to your doctor first. Activities that may affect the pump are:

  Deep heat therapy (diathermy)

  Hyperbaric chamber treatment

  Scuba diving

  Saunas

  Heating pads placed over the pump site

  Steam baths

  Mountain climbing

  Travel in non-pressurized aircraft

- Notify your clinic if you plan to travel far from home for long periods of time. Your doctor will tell you if you need any changes to your prescription and work with you to coordinate any care or refills you need during your trip.
- Make sure your family members know you have an infusion system so they can inform medical personnel in an emergency.

Common Questions

Will this therapy cure my condition?

The medication your doctor has prescribed may or may not cure your condition. Your infusion system is just a tool your doctor will use to deliver your medication continuously to a specific location in your body. Your doctor may give you additional medication.

Will my infusion system be noticeable?

Depending on your body size and shape, and on the pump's location, it will likely not be noticeable through your clothes.

Will my infusion system need to be replaced?

Probably not. There are no electrical parts that wear out within the pump. If the catheter becomes blocked, kinked, or torn, the catheter may need to be replaced.

Can I stop taking other medications once I have the infusion system?

Your doctor will decide if you need to take other medication. To prevent any negative side effects, do not make any changes in your current medication unless your doctor has told you to do so.

Will my infusion system prevent me from traveling?

The infusion system will not prevent you from traveling, but be sure to schedule and keep all refill appointments. Notify your clinic if you plan to travel far from home for long periods of time. Your doctor will tell you if you need any changes to your prescription. Your doctor will work with you to coordinate any care or refills you need during your trip.

Will flying affect my infusion system?

Flying in commercial airlines will not generally affect the pump. However, talk to your doctor before taking flights in non-pressurized aircraft.

Will my infusion system set off the metal detector at the airport?

The pump may set off the metal detector. If it does, show your Patient Identification Card to airport security.

Will I be able to take hot baths or showers?

Yes. A hot bath or shower is unlikely to interfere with the pump's operation. However, talk with your doctor first if you plan to engage in activities that may greatly affect the temperature or pressure of the pump. Such activities include steam baths, saunas, heating pads placed over the pump site, deep heat therapy (diathermy), hyperbaric chamber treatment, and scuba diving.

Can I have an MRI with an infusion system?

Although Magnetic Resonance Imaging (MRI) should not affect your pump operation, you may experience a slight tugging sensation of the pump or warmth in the area directly surrounding the pump in the MRI environment. An elastic garment or wrap will reduce the tugging sensation you may feel. If the warming sensation is uncomfortable for you, the MRI settings can be adjusted to reduce or eliminate the warming sensation you may feel.

Contact your doctor or the physician who implanted your pump before having an MRI performed so that they can discuss the procedure with the MRI staff to determine if it is safe and appropriate for you.

What about radiation therapy or lithotripsy?

The effects of radiation therapy and lithotripsy are unknown. Talk to your doctor before scheduling any additional therapies or diagnostic tests. Your doctor will decide if you need to take any precautions.

The Identification Card

Your doctor will give you a temporary identification card which should be filled out and carried with you. After Medtronic receives your device registration information from the hospital, you will receive a permanent identification card. The identification card has important information about your pump.

Carry your Identification Card with you at all times.

In case of emergency, the card will give those attending to you information about your pump, your doctor's name, and important phone numbers.

If you lose your identification card or need to change information on your existing card, contact:

Patient Services
Medtronic Neurological
800 53rd Avenue NE
Minneapolis, MN 55421
Toll-Free: (800) 510-6735

Glossary

Catheter — The small, flexible tube that connects to the pump. The pump delivers medication through the catheter to the location in your body where it is likely to be most effective.

Reservoir Fill Port — The raised port in the center of the pump. To refill your pump, your doctor or nurse inserts a needle through your skin and through this port into the reservoir.

Flow Rate — The amount of medication the pump delivers over a specific time.

Pump — A round, metal disk that stores and releases prescribed amounts of medication into your body.

Pump Drive — The gas that pressurizes the reservoir and forces the medication out.

Reservoir — The space inside the pump that holds the medication.

Reservoir Size — The amount of medication the pump can hold.

Septum — The silicone stopper through which your doctor fills the pump or accesses the catheter directly.

Catheter access port — A port near the edge of the pump. It allows your doctor to inject medications or solutions directly into the catheter.

Important Names and Numbers

Ask your doctor or nurse to complete the information on this page:

Pump model: _____

Pump reservoir size: _____

Pump flow rate: _____

Serial number: _____

Surgery date: _____

Doctor's name: _____

Nurse's name: _____

Follow-up clinician's name for refills/check-ups: _____

Number to call for appointment: _____

You are receiving the following medication:

_____

If you experience any of the following symptoms, please contact your doctor: _____

_____

_____

_____

_____

_____

_____

Refill Schedule

January	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31
February	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29
March	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31
April	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30
May	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31
June	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30
July	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31
August	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31
September	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30
October	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31
November	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30
December	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31

Questions I Want to Ask My Doctor or Nurse

Notes

Medtronic

When Life Depends on Medical Technology

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