PATIENT GUIDE

For use with Prometra® II Programmable Pump System

MR Conditional

Caution: Federal Law (USA) restricts this device to sale by or on the order of a physician.

Table of Contents

Glossary

Abdomen: soft space between your ribs and hip bones
Arachnoid: the middle protective membrane covering the brain and spinal cord
Anesthesia: medicine that causes you to lose your ability to sense pain, among other sensations
Bolus: large or concentrated dose of medicine
Cardioversion: electrical "jump start" for your heart to correct irregular rhythms. Also may be done with medication(s).
Catheter: tiny flexible tube
CSF: cerebrospinal fluid
Chronic: long-term
Contrast media: dye that can be seen under x-ray
CT: non-invasive, non-magnetic scan used to verify intrathecal catheter position
DEHP: Bis(2-ethylhexyl)phthalate, a plasticizer in PVC
Defibrillation: stopping the heart from quivering, "fibrillating", instead of pumping normally. Often done by applying electricity via small paddles but may also be done with medication(s).
Dura Mater (Dura): the outermost protective membrane covering the brain and spinal cord
Epidural: located outside the dura mater or anesthesia injected into this space.
Explant: to take out; opposite of implant
FDA: US Food and Drug Administration
Fiddling: rotating the pump in the pocket created for it in the abdominal wall
Hyperbaric: the medical use of oxygen at a level higher than atmospheric pressure.
Implant: to put in
Inflammatory mass: group of inflamed cells
Intractable: difficult-to-manage; hard to treat, relieve, or cure
Intrathecal space: fluid-filled area around the spinal cord
Latex: natural rubber
Orally: by mouth
Palpable: that which can be felt by touching
PVC: polyvinyl chloride, a plastic material
Programmable: ability to be controlled remotely
Prometra: brand name for Infusyn Therapeutics' programmable drug delivery pump and pump system
Saline: Salt water balanced to match your body's composition
Telemetry: remote transmission of data
Vertebra/Vertebral Body: bones or segments which make up the spinal column and through which the spinal cord runs

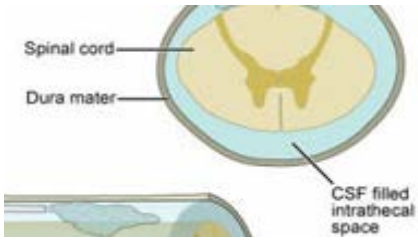
Descriptive Information

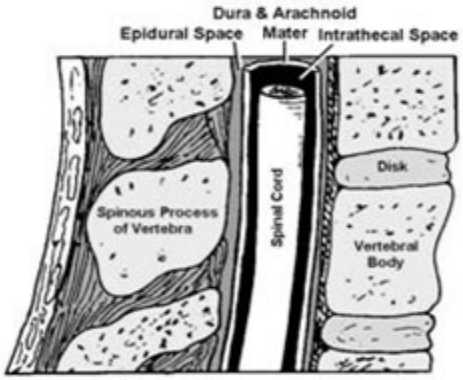
Your doctor is recommending this treatment for you because your prior treatments have not been adequate. This Patient Guide will help you understand your Prometra II Programmable Pump System and help answer your questions about this treatment. However, it is only a guide and **your doctor and nurse are always your best source of information**. Be sure to ask them to explain anything that is unclear. And, always follow their directions concerning your Prometra II Programmable Pump System.

Note: The use of the terms "medication" and "drug" throughout this document refer to the use of Infumorph® which is the Food and Drug Administration (FDA) approved brand name for Morphine Sulfate or baclofen injection (intrathecal).

Potential Benefits of the Prometra II Programmable Pump System

Your spinal cord is the main pathway for information connecting your brain and all the rest of the nerves in your body. If you take a pill orally (by mouth), medicine has a much harder time reaching the spinal cord as much of the drug is absorbed by your body along the way. Delivering this dose directly to your spinal cord reduces the amount of medication needed. For example, published studies show that you can take 1/100th of your pain medication when it is delivered to your **intrathecal space (fluid-filled space around your spinal cord)** and achieve the same result.[1] With a much smaller intrathecal dosage, your side effects may be reduced. Or, your doctor may be able to increase your dosage without as many side effects.





Purpose of the device (FDA approved indications for use)

The Prometra® Programmable Infusion Pump System is indicated for intrathecal infusion of drug therapy, including: Infumorph ® (preservative free morphine sulfate sterile solution), preservative-free sterile 0.9% saline solution (Sodium Chloride Injection, USP), and baclofen (baclofen injection, intrathecal, 500-2000 mcg/mL). For Infumorph, the pump system is indicated for use in patient

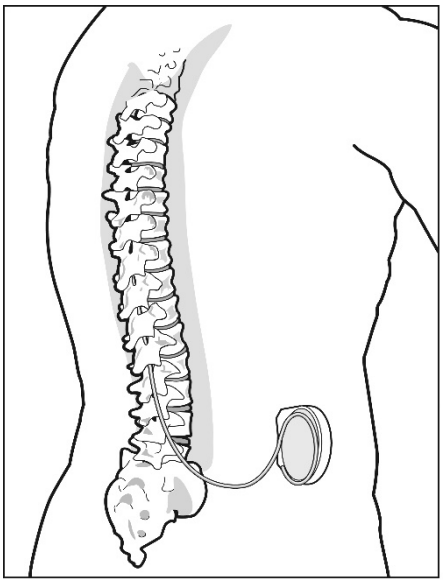
[1] Rauck R, Intrathecal drug delivery. Seminars in Pain Medicine, 2004; 2(1): 2-7.

populations of 22 years and older (adults). For baclofen and 0.9% saline solution, the pump system is indicated for use in patient populations of 12 years and older (adolescents and adults).

The approved drug labeling governs the indications, contraindications, warnings and precautions related to the use of the drug. The National Library of Medicine at www.nlm.nih.gov is a good source for this information.

Description of the device

The **Prometra II Programmable Pump System** infuses the drug directly to your spinal cord.



A thin **intrathecal catheter** with holes near the end is carefully placed in your intrathecal space and securely connected to the Prometra II programmable pump implanted in your abdomen (the soft space between your ribs and hip bones). Your catheter has a radiopaque tip that can be seen under x-ray.

The pump has a central refill septum that a nurse or doctor can feel underneath your skin (palpate). Your medicine will be refilled every 30-90 days by accessing this refill port with a thin needle. If needed, the nurse or doctor may access your catheter directly to provide a bolus (large or concentrated dose) of medicine through the catheter access septum.

When you initially receive the pump, and at most refills, the nurse or doctor will use a handheld programmer, like a remote control, to set how much medicine to deliver and at what times. Your programmable pump can deliver different amounts of medication at different times of the day, such as more at night while you are sleeping and less during the day.

Prometra Clinician Programmer

Making the Decision if the Pump is Right for You

Contraindications

The pump system should not be implanted:

- If you have an infection, such as a tooth abscess or a bed sore.
- If your body type cannot comfortably or safely accommodate the pump size and weight.
- If the pump cannot be implanted under your skin 2.5 cm (1 in.) deep.

- If you have allergies to the catheter materials, including silicone elastomers, barium sulfate, tungsten, polyacetal resin, ink, stainless steel, hydroglide hydro gel coating, or plastic needle hubs (polypropylene and acrylic based).
- If you have allergies to the pump materials, including titanium, silicone elastomers, polyphenylsulfone, silicone adhesive, polyvinylidene fluoride, MP35N metal (nickel-cobalt-chromium-molybdenum alloy), or stainless steel (AL29-4, 316L).
- If you have exhibited a prior intolerance to implanted devices.
- If your spinal column anatomy obstructs cerebrospinal fluid flow or prevents intrathecal drug delivery.
- If you are deemed an unsuitable candidate after psychological evaluation.
- If you have any contraindication to Infumorph or baclofen injection (intrathecal) as per the approved drug labeling. The National Library of Medicine at www.nlm.nih.gov is a good source for FDA-approved drug information.

Warnings

WARNING: USE OF UNAPPROVED DRUGS (e.g., DRUG COCKTAILS, PHARMACY-COMPOUNDED DRUGS, MORPHINE WITH PRESERVATIVES, ETC.) WITH THE PROMETRA II PUMP COULD RESULT IN PUMP FAILURE AND/OR SERIOUS ADVERSE EVENTS SUCH AS SEVERE UNDERDOSE, OVERDOSE OR DEATH.

WARNING: FAILURE TO EMPTY THE PUMP PRIOR TO EXPOSURE TO MRI ENVIRONMENT COULD RESULT IN DRUG OVERDOSE THAT COULD LEAD TO SERIOUS PATIENT INJURY OR DEATH. THE PUMP MAY NEED TO HAVE AS MUCH AS 20ML OR 40ML OF DRUG REMOVED DEPENDING ON THE PUMP TYPE AND MODEL NUMBER.

- You should not undergo hyperbaric therapy since exposure could result in drug underdose.
- In the event of over-medication, refer to the approved drug labeling for appropriate treatment.
- Clinicians implanting, programming, accessing, or maintaining implanted programmable pumps must comply with the instructions for use. Technical errors may result in a return of underlying symptoms, drug withdrawal symptoms, or clinically significant or fatal overdose.
- Do not incinerate or cremate the pump.
- You should not have an occupation where you would be exposed to high current industrial equipment, powerful magnets or transmitting towers, such as, electricians, electrical engineers or MRI technicians.

Magnetic Resonance Imaging (MRI) and Safety Information

MR Conditional

WARNING: FAILURE TO EMPTY THE PUMP PRIOR TO EXPOSURE TO MRI ENVIRONMENT COULD RESULT IN DRUG OVERDOSE THAT COULD LEAD TO SERIOUS PATIENT INJURY OR DEATH. THE PUMP MAY NEED TO HAVE AS MUCH AS 20ML OR 40ML OF DRUG REMOVED DEPENDING ON THE PUMP TYPE AND MODEL NUMBER.

Avoid powerful magnets, such as MRI without first seeing your pump management doctor. Strong magnetic fields, such as those created in Magnetic Resonance Imaging (MRI) devices may cause the valves of the pump to open, resulting in the immediate discharge of the contents of the pump and catheter into your body which could result in a fatal overdose.

If an MRI is required, your doctor **MUST** completely empty your pump of all medication prior to the MRI. Your doctor may arrange for another method of pain relief while there is no medication in your pump.

Pump performance has not been established for MRI scanners at fields other than 1.5 T (Tesla). You should not have an MRI in any scanner other than a 1.5 T scanner under the conditions listed on your implant card.

You should inform your doctor who manages your pump if you are going to have an MRI. Your doctor will recommend whether or not an MRI is appropriate for you and ensure that your pump has been properly emptied and programmed to zero (0) flow prior to the procedure.

Make sure to inform the MRI technician that you have an implanted Prometra II Programmable Pump prior to entering an MRI scanner. To make this easy for you, a medical bracelet and implant card have been provided to you. These both have the phone number (855-356-9665) to call before an MRI scan to obtain the safe scanning conditions.

Your implant card and medical bracelet should be with you at all times. **You will be asked at the MRI facility to remove all jewelry and your medical bracelet prior to entering an MRI scanner.** Remember your medical bracelet, like other jewelry, contains metal and could cause burns where it contacts your skin. Thus, these must be removed prior to scanning.

During an MRI, you may notice a warming sensation around the pump or feel a tingling sensation. If the warming or tingling sensation is uncomfortable to you, the MRI should be stopped and the settings adjusted to reduce or eliminate the sensation.

During an MRI, you may also notice a tugging sensation at the pump. An elastic wrap can be used to reduce the tugging sensation.

Additionally, the metal in the pump will cause the MRI image to be distorted in the area around the pump. The MRI should be adjusted to minimize the image distortion.

After the MRI, your doctor will confirm the status of your pump and may require close monitoring after refilling the pump with medication to ensure the pump is operating properly.

It is recommended that you register the MRI conditions under which your implant can be scanned safely with the MedicAlert Foundation (www.medicalert.org).

Precautions

General:

- Carefully read all instructions prior to use. Follow all instructions.
- Certain equipment may cause electrical noise, which may interfere with programming. If suspected, move the patient from the suspected source of interference to facilitate the programming procedure. Examples of equipment that may cause inference include: radio, TV, cellular phones, telemetry, amateur radio, radio navigational aids, industrial scientific medical devices (ISM), large electric motors, etc.
- Do not use accessories that are not referenced in these instructions for use. Only use devices and accessories that are referenced for use with the Prometra II® Programmable Pump in these instructions.
- Safety and effectiveness for use in pediatric patients with Infumorph under 22 years old has not been investigated or established.
- Safety and effectiveness for use on pediatric patients with baclofen below the age of 12 has not been investigated or established.
- The effects of implanting this device in patients with other implanted medical devices, other than neurostimulators, are unknown.
- Pain on injection that was not noted during previous injections may be an early sign of infection.

Implant:

- Implantation of this device and subsequent use, reprogramming, and refill should only be conducted by qualified medical personnel specifically trained for surgical implantation, use, and maintenance of the device. Use of this device by non-qualified or untrained personnel could lead to serious consequences involving under- or over-medication. In the event of over-medication, refer to the approved drug labeling for appropriate treatment.
- If therapy is discontinued for an extended period, the pump should be emptied of drug and filled with a preservative-free 0.9% sterile saline solution and programmed to a low infusion rate to maintain catheter patency.

- In the pediatric population, care must be taken to select an appropriate location, taking into consideration available body mass, presence of ostomies, growth development, and co-morbidities.

Device Compatibility:

- **Pump accessories.** Only use the Prometra II Programmable Pump with the accessories listed in these instructions for use. Use of alternate accessories may result in damage to Prometra II components, less than adequate therapy, or increased risks to the patient.
- **Pump.** Only use with Prometra Programmer.
- **Therapeutic ultrasonics or lithotripsy -** Use of therapeutic ultrasonic devices, such as electrohydraulic lithotriptors, has not been tested on the Prometra II pump. If lithotripsy must be used, do not focus the beam in proximity of the pump.
- **Medical devices**. The Prometra Pump Programmer may affect other medical devices. Use or interference with medical devices, other than neurostimulators, has not been established.
- **Applied electric currents.** Interaction of the Prometra II Pump with electric currents applied to the body such as cardioversion or defibrillation has not been established. Care must be exercised if you receive these treatments. Where practical, the pump should be turned off before application of electric currents to your body. Confirmation that the pump programming has not changed must be carried out as soon as possible after the procedure.
- **Radiation.** Do not use radiation therapy in the area of the pump. The effects of ionizing radiation on the Prometra II Pump have not been established, and these therapies may have effects on pump operation that are not immediately apparent.

Risks

Potential Adverse Events

Since the Prometra II Programmable Pump System may remain implanted for ten (10) or more years, take time to familiarize yourself thoroughly with the therapy and take an active role in your outcome.

Because the pump and catheter are placed during a surgical procedure, surgical complications may occur. Always discuss the potential risks and benefits of this therapy with your doctor and ask any questions that you have.

The potential exists for serious complications including the following:

Possible Risks Associated with Programmable Implantable Pump

- Adverse reaction to pump materials
- Battery depletion
- Bleeding
- Body rejection phenomena
- Defective pump (e.g. propellant chamber leakage, pump rupture)
- Inability to locate septum

- Inability to program pump due to programmer failure or loss of telemetry
- Inflammation, necrosis, or scarring of skin over implant area
- Programming errors, resulting in over or under dosing
- Pump flipping or twisting
- Pump implanted too deep, resulting in difficulty accessing or inability to access port
- Pump migration (moving within your body)
- Pump pocket pain/soreness
- Pump pocket seroma/hematoma, with or without infection
- Pump rotation
- Pump site skin erosion (pump rubs through your skin)
- Pump stoppage
- Refill errors, including injection into pump pocket, injection into wrong port, incorrect volume, incorrect concentration, difficulty accessing pump port
- Septum dislodgement
- Septum leakage
- Slow, erratic or fast flow
- Software error

Possible Risks Associated with Intrathecal Catheter

- Catheter disconnection
- Catheter kinking
- Catheter fracture
- Catheter migration (moving within your body)
- Cerebrospinal fluid (CSF) leak
- Disconnection
- Erosion (catheter rubs through your skin)
- Fibrosis (scarring)
- Infection in intrathecal space, including meningitis
- Inflammatory mass formation (e.g., granuloma)
- Malpositioning
- Nerve damage
- Pain on injection
- Poor radiopacity
- Post dural puncture headache (post surgical headache)
- Reaction to catheter materials
- Reversible or irreversible partial or complete occlusions (blockages)
- Spinal cord pressure leading to paralysis
- Spinal cord trauma, perforation, laceration
- Subcutaneous catheter tract infection
- Subcutaneous tunnel infection
- Tears/breaks

In rare instances, the development of an inflammatory mass at the tip of the implanted catheter may occur, which can result in serious neurological impairment. Patients should be monitored carefully at each visit for any new neurological signs or symptoms, including:

- 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

- Burning, numbness, or tingling
- Increase in pain despite dose escalation
- Increased sensitivity to stimuli or pain
- Progressive change in the type or amount of pain
- Bowel and/or bladder dysfunction
- Gait disturbances or difficulty ambulating
- 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 a CT scan with contrast) and appropriate clinical consultation.

Inflammatory mass has been associated with a wide range of doses and concentrations of opioids. No dose or concentration of Infumorph can be considered completely free of risk from inflammatory mass. The risk of inflammatory mass occurrence appears to be cumulative over time and increases with higher concentrations and doses of opioids.

Potential Side Effects of Infumorph

- If nausea occurs, consult your doctor or pharmacist for ways to decrease it (such as taking antihistamines, lying down for 1 to 2 hours with as little head movement as possible).
- This medication may cause dependence, especially if it has been used regularly for a long time or in high doses. In such cases, withdrawal reactions (such as restlessness, watery eyes, widened pupils, sweating, and runny nose) may occur if you suddenly stop this drug. To prevent withdrawal reactions, your doctor may reduce your dose gradually. Consult your doctor or pharmacist for more details, and report any withdrawal reactions immediately.
- When this medication is used for a long time, it may not work as well. Your doctor may need to increase your dose or change your medication. Talk with your doctor if this medication stops working well.
- Along with its benefits, this medication may rarely cause abnormal drug-seeking behavior (addiction). This risk may be increased if you have abused alcohol or drugs in the past. Use this medication exactly as prescribed to lessen the risk of addiction.
- Tell your doctor if your pain persists or worsens.

- Nausea, vomiting, constipation, lightheadedness, dizziness, drowsiness, increased sweating, or dry mouth may occur. Pain, redness, or swelling at the injection site may occur if this medication is given into a muscle or under the skin. If any of these effects persist or worsen, tell your doctor or pharmacist promptly.
- To prevent constipation, maintain a diet adequate in fiber and drink plenty of water, if not contraindicated. If necessary, consult your doctor for help in selecting a laxative (such as a stimulant type with stool softener).
- Remember that your doctor has prescribed this medication because he or she has judged that the benefit to you is greater than the risk of side effects. Many people using this medication do not have serious side effects.
- Tell your doctor immediately if any of these unlikely but serious side effects occur: slow/shallow breathing, fainting, mental/mood changes (such as agitation, hallucinations, confusion), difficulty urinating, vision changes, slow/fast heartbeat.
- Tell your doctor immediately if any of these rare but very serious side effects occur: severe stomach/abdominal pain, change in the amount of urine, seizures.
- A very serious allergic reaction to this drug is rare. However, seek immediate medical attention if you notice any symptoms of a serious allergic reaction, including rash, itching/swelling (especially of the face/tongue/throat), severe dizziness, trouble breathing.
- This is not a complete list of possible side effects. If you notice other effects not listed above, contact your doctor.

Potential Side Effects of baclofen injection (intrathecal):

Careful attention to the programming and monitoring of the pump is required to prevent some of the risks and problems associated with baclofen injection (intrathecal). To decrease these risks you must go to regular follow-up visits and always follow your doctor's instructions.

Potential side effects with baclofen injection (intrathecal) include:

- The drug not being effective in managing your symptoms
- Remember that your doctor has prescribed this medication because he or she has judged that the benefit to you is greater than the risk of side effects. Many people using this medication do not have serious side effects.
- Sweating, diarrhea, constipation, rash, emotional problems, abnormal thoughts and sudden change in personality, headache, dizziness, seizures, stroke, slow or fast breathing, pneumonia, pulmonary embolus (a blood clot in the lung), sudden decrease or increase in blood pressure, slow or fast heart rate, palpitations, abnormal heart rhythm, urine retention, kidney failure, increased muscle tone, decreased muscle tone. If you experience any of these side effects, tell your doctor or pharmacist immediately and consider that there may be a drug overdose which would require emergency medical treatment.
- This is not a complete list of possible side effects. If you notice other effects not listed above, contact your doctor or pharmacist.

Serious Side Effects of baclofen injection (intrathecal):

Serious Side Effects can occur due to an over-dose, under-dose, or sudden stoppage of baclofen injection (intrathecal) delivery. **Seek emergency medical attention immediately if signs of under/overdose appear:**

- Early symptoms of **under-dosing or withdrawal** of baclofen injection (intrathecal) can be return to baseline spasticity, itchy skin, low blood pressure, and generalized "pins and needles" in your skin.
- Signs of **overdosing** can be drowsiness, lightheadedness, dizziness, slow or difficult breathing, seizures, and loss of consciousness that could lead to a coma.
- **Abrupt withdrawal of baclofen injection (intrathecal) may be life-threatening.** Signs of a sudden stop of baclofen injection (intrathecal) flow (or "abrupt withdrawal") into your spine can be: high fever, change in mental status (this might include confusion, amnesia, poor judgment, drastic mood changes), and sudden increase in spasticity. If you do not receive medical treatment, the sudden stop of baclofen injection (intrathecal) flow could result in breakdown of muscle tissue, multiple organ failure, and death.

Benefits

Implantation of the Prometra II programmable pump system is often used when conventional treatment is no longer effective. Benefits you may expect include:

- Less need for oral medications
- Accurate delivery of the prescribed dosage

Before, During and After Your Procedure

Your Pump Implant Surgery

The Prometra II Programmable Pump System will be placed in your body during a surgical procedure that is usually about 1 hour long. You will be given anesthesia which will allow you to sleep through the surgical procedure without pain. Your doctor will give you specific instructions about how to prepare for the surgery.

Both the pump and catheter are implanted under your skin. A small incision is made in your back to provide access to your spinal canal. The tip of the catheter is threaded up your spine into your intrathecal space while using a form of x-ray. Your doctor usually places the pump at about waist level (abdomen), above your hip bone and below your ribs, and to one side. The catheter is tunneled underneath your skin from where it enters your spine around your waist to the pump. The catheter length is then customized to your body and connected to the pump. Your doctor may choose to use sutures near where the catheter enters your spine. This will help the catheter to maintain its position.

Your pump will be filled and programmed to deliver your medication at either a constant or variable rate, or it can be set to give a dosage repeated at specified times. Your doctor will determine the best medication schedule for you.

When you wake up, you will notice two incisions. Your doctor made one incision in your abdomen to place the pump. Another small incision is made in your back to position the catheter in your spine.

Follow-up Visits

Your first follow-up visit will be scheduled one to two weeks after surgery. At this visit, your doctor will look at the surgical site and review the medication therapy plan that was started when you received your pump.

Refills

Your doctor will schedule regular pump refill visits as needed so that your pump does not run out of medication. This is usually about every 30-90 days. Only your doctor or nurse can program your pump to deliver medication. **It is important not to miss a refill appointment.** You should always let your doctor know as soon as possible if you think you will miss an appointment. This will allow time for a new appointment to be set or for other arrangements to be made. **If your pump is not refilled on time, it may become empty, and you will not get your required medicine. When you run out of medicine, your symptoms can range from fairly minor to very serious depending on the medicine you were receiving, such as with baclofen injection (intrathecal), serious risks can occur due to a sudden stop in drug delivery.** Refer to the drug's prescribing information for the withdrawal or underdose symptoms. Your doctor can describe the symptoms to expect if your pump runs out of medication or if you stop getting medicine from the pump for any reason.

To refill your pump, your doctor will insert a special needle of just the right size and length into your pump through the center refill septum. For most patients this causes only a mild pricking sensation. Then, your doctor or nurse will completely empty your pump. Your pump must be emptied to measure the amount of medication that was left in the pump. This allows verification that the pump has been delivering the right amount of medicine to your spinal cord. Your doctor will then refill your pump by attaching a syringe and tubing set filled with your medication to the special needle and pushing the medication into the pump reservoir. Then, your doctor or nurse will program the pump to deliver your medication using the programmer. Once the pump is refilled and programmed by your doctor, the pump will automatically deliver the medication at the programmed dosage rate.

What should I expect after surgery?

After surgery you may have some redness and tenderness in the area where your incision was made. This will normally go away in a few weeks. However, contact your doctor or nurse if you notice unusual changes in the skin area over the pump such as increased swelling, redness, or soreness.

For the first few days after you receive the pump, you should avoid heavy exertion and strenuous activities such as lifting or pushing, carrying anything heavy, running, and swimming. Follow all your doctor's instructions about your pump. Once your incision heals, you should be able to resume normal daily activities such as bathing and exercising.

Will I need to wear a bandage over the pump?

A bandage will be required until your incision heals. After a refill visit, a bandage may be used over the area where the needle was inserted.

Will others know that I have a pump?

After your incision heals, the pump will likely protrude slightly from your abdomen. In thinner people, it tends to protrude more and in larger people, it is less obvious. Your doctor may be able to provide pictures of what the pump looks like in different body types.

Do I have to wear certain types of clothing?

This depends on where your pump is placed. You should avoid clothing that would rub or be tight over the incision site immediately after surgery. Wear loose, comfortable clothing the day of your implant surgery. After the incisions heal, you should be able to wear your normal clothing.

Can I move my pump, e.g. if it is uncomfortable?

Your pump has been placed with the refill septum facing up so it can communicate with the programmer in your doctor's office. Never move, twist or turn your pump (fiddling). This may flip your pump or cause damage to the catheter. Either of these may interfere with delivery of your medication or require reoperation. However, typical movement should not result in damage to the catheter or pump.

How do I know if my pump still works after I bump it or if I fall? What about my catheter?

A slight bump is unlikely to affect your pump or catheter. However, if you hurt yourself when you fell, you may have hurt the pump or catheter. If you experience much more pain or notice unusual symptoms, contact your doctor immediately. To verify if your pump and catheter are working, your doctor or nurse will check the amount of medication left in the pump. If too much is left, they may perform an x-ray or CT to verify proper catheter and pump position.

Will my pump set off metal detectors? Is security "wanding" safe?

It may. And, as some personnel are not familiar with the implant card with which you will be provided, you may be asked to show them the pump site. Please consider this when dressing for court appointments, air flights and other facilities where metal detectors might be encountered. If you need to be "wanded" by security personnel, e.g. at the airport, the pump programming will not be affected.

What should I do if I hear my pump beeping or making noise?

Your Prometra II programmable pump has two alarms. Both alarms use the same beeping tone but have a different beep length and different number of beeps in a group. **Contact your doctor immediately if you hear these alarms.**

The **Low Reservoir Alarm** warns you when the medication in the pump reservoir gets below a certain volume. Your doctor can set this volume, and the alarm can be turned on using the programmer. If the alarm is on and the reservoir volume gets low, the pump sounds two short beeps every 30 minutes. The alarm continues to sound until your doctor turns it off using the programmer or refills your pump.

The **Critical Error Alarm** indicates that the pump has stopped delivering medication. The pump sounds three long beeps every 30 minutes. This alarm occurs any time the pump is not delivering medication, including a low pump battery. Once the **Critical Error Alarm** has occurred, the pump stops pumping medication. Your doctor cannot turn off the alarm with the programmer. Your pump will keep beeping until it is replaced or until the battery runs completely out of power. There is no way to replace the battery only. The pump must be disconnected from the catheter and replaced. A new pump can be implanted and connected to the original catheter. Contact your doctor as soon as possible to schedule pump replacement surgery or to assess therapy alternatives.

Will the use of cell phones, a microwave oven, or other household electrical devices interfere with my pump?

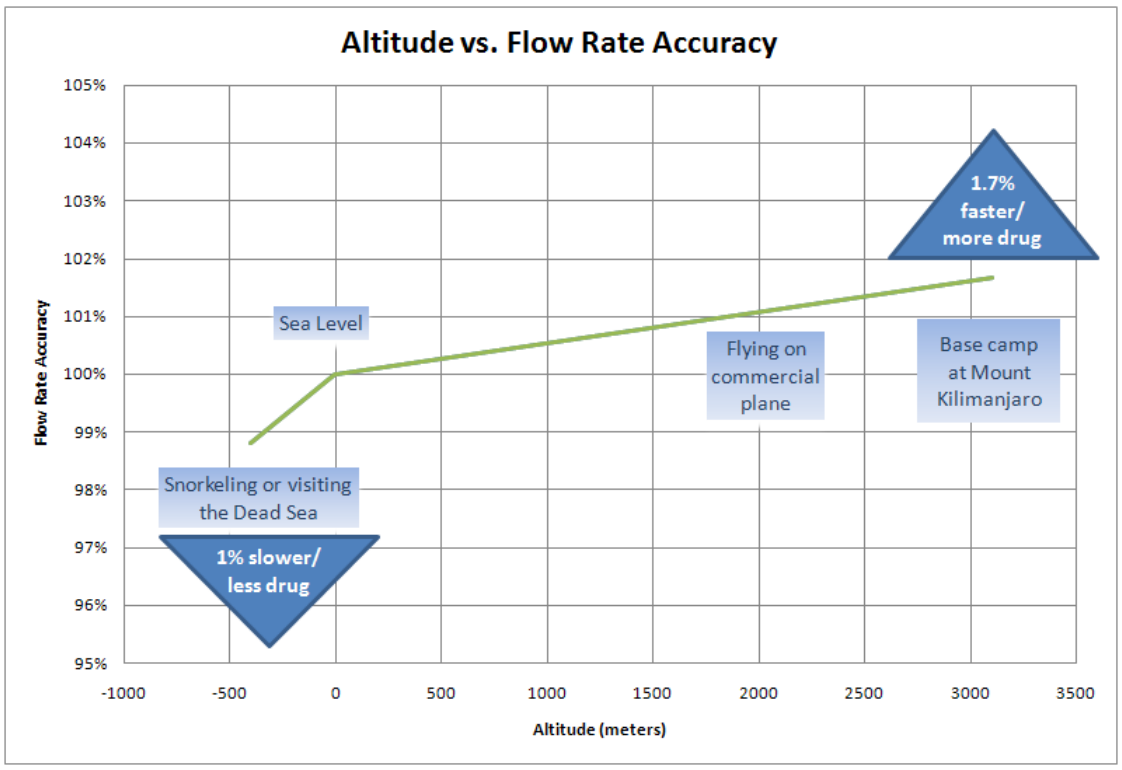
No. Your pump is designed so that cell phones, microwaves, or other household appliances and items that you may use in your normal daily life will not affect it. If you suspect interference with your pump, move away from or turn off the electrical device. Your pump will not be permanently affected.

Do pressure changes affect my pump?

The Prometra II programmable pump has a special design which isolates the drug reservoir from most pressure changes, making it ***immune to most pressure changes***. You are free to enjoy, with your doctor's permission:

- Flying
- Mountain hikes up to 10,000 feet
- Skiing up to 10,000 feet
- Snorkeling within 15 feet of the surface
- Swimming within 15 feet of the surface

These activities are SAFE and WILL NOT AFFECT YOUR PUMP. Always consult your doctor first about any other activities not listed here.



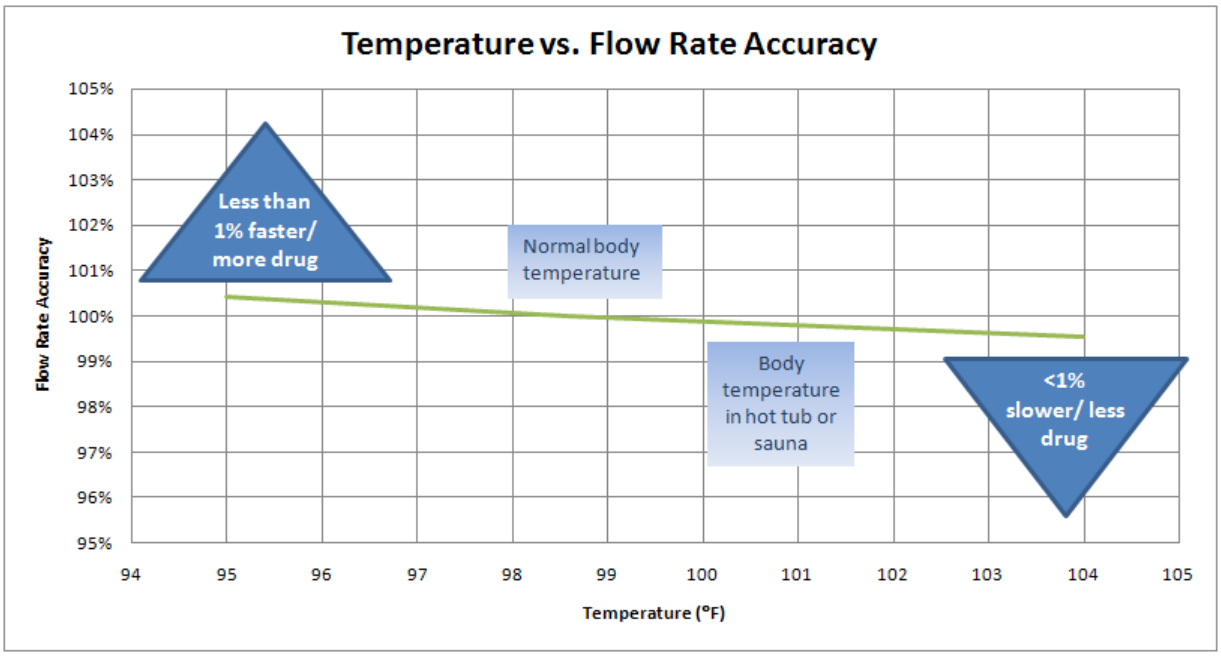
Activities such as scuba diving or hyperbaric therapy may cause the pump to temporarily stop delivering drug. When you return to normal atmospheric pressure, your pump will resume its programmed drug delivery. Discuss these activities with your doctor to see if you can safely be without your drug during scuba diving or hyperbaric therapy.

Do temperature changes affect my pump?

The Prometra II programmable pump has a special design which isolates the drug reservoir from most temperature changes, making it ***immune to most temperature changes***. You are free to enjoy, with your doctor's permission:

- Hot tubs
- Whirlpool baths
- Saunas

These activities are SAFE and WILL NOT AFFECT YOUR PUMP. Always consult your doctor first about any other therapies not listed here.



Even temperature-related therapies such as deep heat therapy, e.g. diathermy, will not affect the operation of the pump. Always consult your doctor first about any other activities not listed here.

Can I travel with my pump?

The Prometra II programmable pump provides you with the freedom to travel. Let your doctor know if you plan to travel so that pump refill arrangements can be made, if necessary. Also, your doctor can advise you of a doctor in the area you are traveling to in case you have any problems.

What should I do if I move?

Contact your doctor to ask for help finding a new pump management physician who can perform your refills. Then, when you have your new address, please contact **Customer Support** at **855-356-9665** so we can update our database in case we need to contact you.

Who do I need to tell about my pump and catheter implant?

You need to tell all medical personnel about your implant. This includes doctors, nurses and medical technicians, such as MRI or X-ray technicians. Knowing about the implant may change their treatment or how they conduct or interpret a medical test. To make this easy for you, you will receive an implant card that contains important information about your Prometra II programmable pump and intrathecal catheter. Your implant card should be with you at all times.

What do I do if I have a question or suspect a problem?

If it is an emergency, always call 911. If you have pain, fever, chills, shortness of breath or dizziness, contact your doctor immediately. Also, contact your doctor immediately if your pain increases or you are experiencing underdose symptoms as this may indicate that your pump may not be delivering drug. If you have any questions or suspect a problem, please contact your implanting or pump management doctor immediately.

Clinical Studies

A. Clinical Study

The performance and safety of the Prometra Pump was examined in an open-label, non-randomized, multi-center study. This study was designed to demonstrate the accuracy and safety of the pump's delivery of Infumorph into the intrathecal space.

The goal of the study was to demonstrate accuracy of drug delivery is within the range of 85-115% through six months post implantation. Additionally the safety profile was evaluated, as determined by the rate of device-related serious adverse events and device complications.

A total of 110 Patients enrolled in the study were implanted with the Prometra Pump. Patients eligible for enrollment were suffering from cancer pain requiring strong opioids, chronic, non-malignant pain, or required an implantable pump system replacement due to malfunction or battery depletion.

Patients were followed monthly for the first 6 months post implantation. During each monthly follow-up visit, the pump was refilled and infused volumes of medication were documented. Drug delivery accuracy and adverse events were documented at the monthly visits.

Results

The goal of the study was achieved. The accuracy of drug delivery was found to be 96.8% with a 90% confidence interval of 95.5% - 97.7%. This met the required range of 85% - 115%.

Adverse Events reported during the study are shown in Table 1.

Table 1: Adverse Events Reported as Possibly, Probably, or Definitely Related to the Device or Study Procedure

System Organ Class	Preferred Term	N (%)
Gastrointestinal Disorders	Nausea	15 (14)
	Vomiting	8 (7)
General Disorders and Administration Site Conditions	Implant Site Pain	20 (18)
	Implant Site edema	11 (10)
	Implant Site Erythema (redness)	9 (8)
	Implant Site Swelling	4 (4)
	Pain	4 (4)
	Implant Site Inflammation	3 (3)
	Drug Withdrawal Syndrome	2 (2)
	Implant Site Hemorrhage	2 (2)
	Pyrexia (fever)	2 (2)
	Tenderness	2 (2)
Infections and Infestations	Incision Site Infection	4 (4)
Injury, Poisoning and Procedural Complications	Procedural Pain	37 (34)
	Post Lumbar Puncture Syndrome	9 (8)
	Wound Secretion	9 (8)
	Seroma (pocket of fluid)	4 (4)
	Wound Dehiscence (re-opening)	3 (3)
Musculoskeletal and Connective Tissue Disorders	Back Pain	2 (2)
	Pain in Extremity	2 (2)
Nervous System Disorders	Headache	8 (7)
	Dizziness	3 (3)
	Intracranial Hypotension	2 (2)
Skin and Subcutaneous Tissue Disorders	Dermatitis Contact	5 (5)
	Pruritus (itching)	2 (2)
	Scab	2 (2)
Surgical and Medical Procedures	Surgery[1]	10 (9)

[1] Surgery to replace or revise intrathecal catheter

Adverse Events with incidence of 1% or less. Tinnitus (ringing in the ears), Abdominal Pain, Constipation, Oral Mucosal Blistering, Catheter Site edema, Implant Site Bruising, Implant Site Effusion, Implant Site Hypersensitivity, Implant Site Irritation, Implant Site Necrosis, Edema Peripheral, Hypersensitivity, Extradural Abscess, Implant Site Cellulitis (infection), Spinal Infection Viral, Excoriation, Hip Fracture[2], Procedural Nausea, Balance Disorder, Burning Sensation, Diplegia (paralysis), Hypoesthesia (loss of feeling), Neuropathy Peripheral (Nerve impairment), Tremor, Dyspnea (shortness of breath), Respiratory Depression, Ecchymosis (bruise), Rash, Hematoma.

[2]Event occurred while patient was being treated with a drug other than Infumorph via Prometra System

B. Use of Intrathecal Baclofen for Patients 12 – 21 years old (Pediatric Use)

There were no new clinical studies conducted to support the use of the Prometra® Programmable Infusion Pump System with Baclofen in the pediatric adolescent patient sub-population (12 years to 21 years). The safety and effectiveness of the Prometra® Programmable Infusion Pump System for the intrathecal infusion of Baclofen in pediatric patients was based on a systematic review of published peer-reviewed literature that evaluated the reported real world clinical performance of currently available implantable intrathecal drug delivery systems (IDDS) used to deliver Baclofen therapy, and on an analysis of Prometra® Programmable Infusion Pump System performance in adults.

Study Design:

Supporting clinical data for this submission was gleaned from the following process:

- Systematic literature review to support expanding to pediatric subpopulations by drawing from the experience with IDDS in children using ITB therapy. The Prometra® Programmable Infusion Pump System is similar in design, technology, performance, indications for use, output characteristics and patient population to currently available IDDS systems.
- Extrapolation of pump performance from adults to pediatric patients by leveraging data gleaned from adult data using the Prometra® Programmable Infusion Pump System as well as data gleaned from reports of baclofen therapy (pediatric and adult use) using currently available IDDS systems.
- Leverage use of pump performance (Prometra®) to deliver pain medication in adults to support baclofen delivery to pediatric patients.
- Assess complication rates of the Prometra® Programmable Infusion Pump in adults.
- Leverage historical analysis of post-market pump performance experience, as reported in the literature, with respect to intrathecal delivery

Literature Search Strategy

The objective of the systematic literature search was to identify applicable publications that contain data on the safety and performance of IDDS for treatment of chronic intractable pain and severe spasticity in the adult and pediatric populations.

The scientific literature databases Medline/PubMed and EMBASE were used by the applicant and duplicated by FDA to perform a search for published data relevant to the clinical evaluation of the Prometra® Programmable Infusion Pump System. The search was conducted for literature published January 1, 2000 through January 1, 2021, to gather both background information and relevant data for the use of intrathecal drug delivery systems (IDDS) for the treatment of chronic intractable pain and severe spasticity in adult and pediatric populations. This data obtained from this literature search has been assessed to be acceptable for use in the statistical analysis to identify the similarity and differences in the IDDS

complications rates across the adult and pediatric populations. Given there is no information on adult patients or pediatric patients receiving Baclofen with the Prometra® Programmable Infusion Pump System, inferential statistics were summarized across pump type, population (adult and pediatric), and type of drug administered to quantify the differences. The primary conclusions from the data analysis are as follows:

- In a relatively modest number of patients, there is no significant difference in the reported events and complications ascribed to the pump between adult and pediatric patients receiving baclofen via other commercially available IDDS.
- When comparing relative risk between adult patients receiving baclofen via other commercially available IDDS and pediatric patients receiving baclofen via other commercially available IDDS, results revealed that pump malfunction requiring explant was higher in the pediatric patients compared to the adult patients (2.8% higher in the pediatric patient). However, the overall reported incidence was relatively low, 3.9%
- Across all of the data collected in the literature search the rate of pump malfunctions in the adult population for other commercially available IDDS did not exceed 4.5% and the rate of pump malfunctions in the pediatric population for other commercially available IDDS did not exceed 4%.

Across the range of 25 individual events and complications, there were differences observed between the adult and pediatric patients with the other commercially available IDDS, but these differences were within the expected differences when the underlying etiology of the patients is considered.

Safety and Effectiveness Results

Safety Results

Taken together, the approved adult baclofen infusion indication and the general clinical information on ITB infusion in adult and pediatric populations, as evidenced from the literature can be used to support safety of the Infusyn Prometra® Pump System for the infusion of baclofen in patients down to age 12. FDA analyzed the complication and adverse event rates reported either in peer-reviewed literature or from post-market surveillance for ITB infusion in pediatric patients, as summarized in the Pediatric Extrapolation section below.

Effectiveness Results

FDA determined the Infusyn Prometra® Pump System is comparatively similar to other currently available IDDS, and the submitted published data generated on patients using these other IDDS systems could be extrapolated to provide information generally on intrathecal infusion of Baclofen in pediatric patients. For example, the relevant device design, method of insertion, and programmable aspects of the devices are similar, and the pumps are a similar size and shape.

Pediatric Extrapolation

The Pediatric Extrapolation Decision Tree provided in the *Guidance for Industry and Food and Drug Administration Staff, Leveraging Existing Clinical Data for Extrapolation to Pediatric Uses of Medical Devices*, issued on June 21, 2016, was used to determine the appropriateness and extent of the extrapolation of clinical data to support a pediatric indication for the Prometra® Programmable Infusion Pump System for the intrathecal infusion Baclofen.

FDA first considered the relevance to the adolescent pediatric population of the clinical information submitted in support of infusion of baclofen in adults using the candidate device. FDA determined there are no relevant differences between adolescent pediatric and adult populations that would require different clinical data with respect to pump insertion, biocompatibility, device performance, or other pump performance parameters. For example, for pediatric patients, the onset, peak response, and duration of action are similar to those seen in adult patients and may vary with individual patients depending on the dose and severity of symptoms[6-10]. In addition, baclofen infusion is currently approved for pediatric patients down to 4 years of age. FDA then considered the expected similarity of response to intervention and quality of data. A summary of these assessments are presented below.

Expected Similarity of Response to Intervention

Question C-1:	*Is the device implanted or in contact with the body, and, if so, does either location or duration of implantation differ between the adult and intended pediatric population in such a way that the safety or effectiveness of the device could be impacted in a clinically meaningful way?*	The device is implanted.
	Does either location or duration of implantation differ between the adult and intended pediatric population in such a way that the safety or effectiveness of the device could be impacted in a clinically meaningful way?	**NO**- The Prometra® Programmable Infusion Pump System is an implantable programmable infusion pump, previously approved for the intrathecal infusion of Baclofen, Infumorph and 0.9% Saline in adults 22 and older. Similar commercially available IDDS have been marketed for use with Baclofen in both the adult and pediatric population. The duration of implantation is the same for adults and the pediatric population[19]. In the pediatric population, care must be taken to select an appropriate pump implant location to accommodate the implantable pump for chronic infusion by taking into consideration available body mass, presence of ostomies, and growth and development[11-16]. To assess the potential difference in the safety and performance of the IDDS in the adult and pediatric

		population, an intra-study summary and comparison of the rate of complications reported in adult and pediatric patients receiving Baclofen with other commercially available IDDS is provided from a retrospective review[18] and a post-market registry[23]. The complication rates for the "Pump Malfunction Requiring Explant" and "Reposition Pump" are 1% higher in the adult population and "Pump Rotation or Flipping, Subsidence or Movement" is 1.7% higher in the pediatric population. Although there are differences seen in the reported complication rates for the pump between the adult and pediatric population, these differences are not statistically different because the 95% confidence limits of the difference included zero. The differences are not considered to be clinically different with no demonstrative impact on the safety to the patient or performance of the pump. To access the potential difference in incidence of pump revisions/post-implantation pump revision between the adult and pediatric the results from a post-market registry[23] for other currently available IDDS were analyzed. The proportion of adult and pediatric patents experiencing the event of interest (intervention following initial implantation) was compared for each 1-year interval following initial implantation. The results indicate that the incidence of intervention was significantly greater in the pediatric patients 1-2 years and 6-7 years post implantation. The author indicates that the risk of surgical revision (number of interventions/ITB naïve patients followed) is highest (adult: 0.112, pediatric: 0.134, cumulative: 0.117) in the first-year post-implant and then rises again in years of anticipated pump replacement. In nonimplant years, surgical revision rates remain low (adult: 0.060, pediatric: 0.073, cumulative: 0.063) relative to published rates and stable. This study had more adult than pediatric spasticity patient, possibility impacting the data. However, after 10 years, 87.2% of the adult and 76.3% of the pediatric patients continued with ITB. The Prometra® Programmable Infusion Pump results were contrasted against the adult and pediatric results presented above. Reported results for implantation during the first year for 738 adult patients and 224 pediatric patients was 11.2% and 13.4%, respectively. Results during the 5th year of implantation revealed an intervention incidence of 6.6% in 332 patients. Comparable results over a similar time frame with the Prometra® Programmable Infusion Pump revealed that the incidence of revisions was 1.2% (24/1,995). Over the 7.5

		years of implantation of the Prometra® Programmable Infusion Pump, from 2013 through the middle of 2020, the incidence of revisions within the first year of implantation has dropped from 4.35% (5/115) in 2013 to 0.40% (6/1,494) in 2020. In aggregate, the total incidence of revisions with the Prometra® Programmable Infusion pump has been 6.58% (611/9,288) suggesting that the Prometra® Programmable Infusion Pump should have comparable incidences of revisions in both the adult and pediatric population as reported for other commercially available IDDS.
Question C-2:	*Are there differences in device characteristics between pediatric and adult use that could impact either device safety or effectiveness in the pediatric population in a clinically meaningful way?*	**NO**- The patient evaluation, pump implantation and therapy maintenance are the same for adults and the pediatric population.
Question C-3:	*Are there characteristics unique to the intended pediatric population that could impact either the effectiveness or safety of the device when used in the pediatric population in a clinically meaningful way?*	**NO-** There are differences in body habitus, subcutaneous tissue and muscle volume and over-size between the adult and pediatric severe spasticity population. In addition, this pediatric population typically suffer co-morbidities including depending on a ventriculoperitoneal (VP) shunt, malnutrition, feeding gastrotomy and severe scoliotic deformities requiring fusion and hardware. These differences have been linked to the higher rate of complications related to the catheter[18]. Comparison of the catheter-related complication rates for other currently available IDDS in the adult and pediatric population revealed that catheter migration, breakage/disruption of the catheter, catheter occlusion, spillage at the time of pull-out, CSF leak/fistula and catheter reposition/advancement were all significantly higher in the patient population. In addition, wound complications (CSF fistula, pseudomeningocele, wound dehiscence, infection) were higher in other currently available IDDS pediatric population when compared to the adult population. The pediatric population is more susceptible to these types of complications due to the decreased amount of muscle and subcutaneous tissue to resist pseudomeningocele formation and wound breakdown[18]. Although there are differences in characteristics unique to the pediatric population with severe spasticity and have been related in increased complication rates related to the catheter and increased wound complications, these events are easily treated, and sequelae is rare. In addition, the benefit of ITB in the pediatric population has been shown to greatly outweigh the risk and negate any clinically meaningful differences[18].

		In conclusion, the differences in characteristics unique to the pediatric population does not impact the effectiveness or safety of the device when used in this population in clinically meaningful way.
Question C-4:	*Are there differences in disease characteristics between adult and pediatric populations that could impact either device safety or effectiveness in the pediatric populations in a clinically meaningful way*	**NO-** Severe spasticity is a conditional that can be caused by many different etiologies (e.g., spinal cords injury, multiple sclerosis, cerebral palsy, traumatic brain injury) and some etiologies may be more prevalent in either population. However, the characteristics of severe spasticity do not differ between the adult and pediatric population. IDDS is a specialized neurosurgical treatment provided to either adult and/or pediatric patients to provide continuous ITB infusion to decrease spasticity. For both populations, the treatment is focused on improving range of motion, facilitating movement, reducing the risk of contracture development and improving quality of life.
Question C-5:	*Are there other differences between adult and pediatric populations that could impact either device effectiveness or safety in the pediatric population in a clinically meaningful way?*	**NO-** The differences between the between the adult and pediatric population identified in C1 – C4 are the only differences that have been identified in the literature.

Data Quality

Question:	*Are the adult data of sufficient quality such that they can serve as a substitute for pediatric data to demonstrate safety or effectiveness?*	**YES-** Three sources of high-quality data was used to support the Prometra ® Programmable Infusion Pump System's pediatric indication for Baclofen: 1. Post-market surveillance data for the Prometra® Programmable Infusion Pump for adult pain management over the last five (5) years. 2. Adult and pediatric (ITB) data from peer-reviewed literature. 3. Prometra® Programmable Infusion Pump clinical performance for the infusion of intrathecal morphine sulfate (Infumorph) in the adult population.

Financial Disclosure

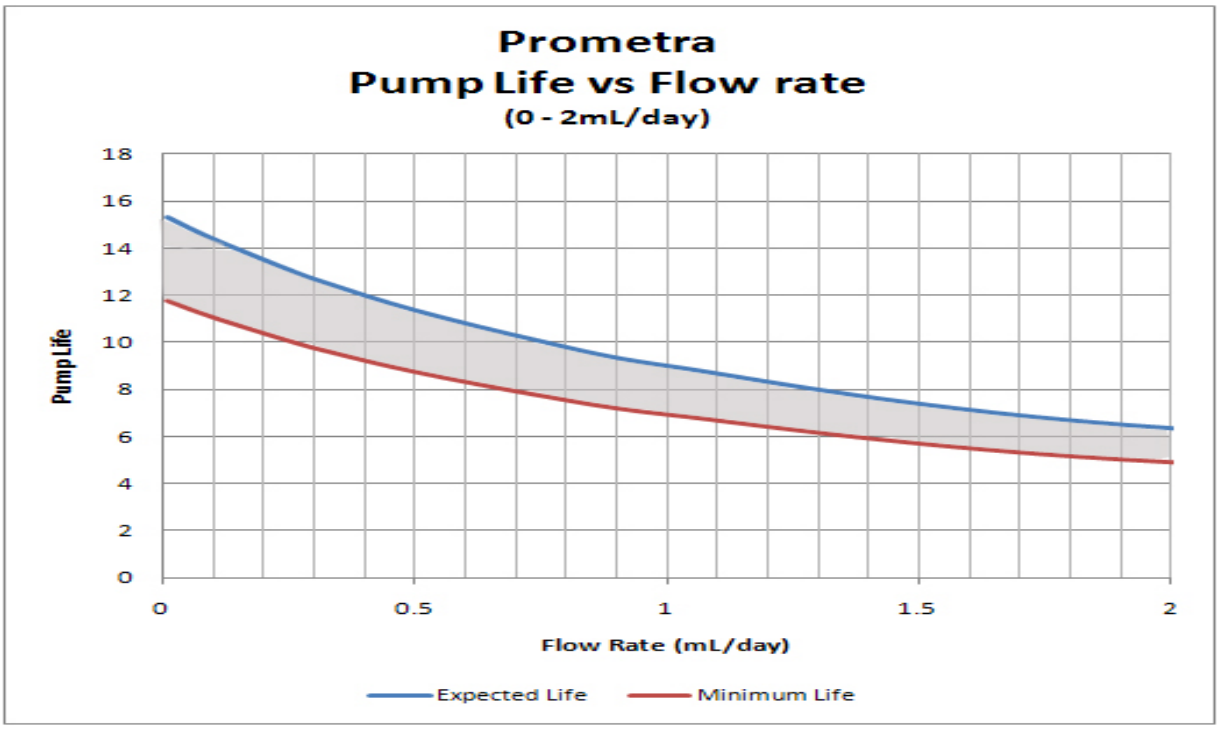
The Financial Disclosure by Clinical Investigators regulation (21 CFR 54) requires applicants who submit a marketing application to include certain information concerning the compensation to, and financial interests and arrangement of, any clinical investigator conducting clinical studies covered by the regulation. The assessment of safety was supported by the PUMP1 study (NCT00817596), which was an IDE study conducted by for study of a different indication but using the same device, was leveraged by FDA in this application for the assessment of safety,

and included 15 investigators. None of the clinical investigators had disclosable financial interests/arrangements as defined in sections 54.2(a), (b), (c), and (f). The assessment of effectiveness was supported by either randomized controlled trials or a peer-reviewed analysis of publicly available post-market data, which in general, are considered to have minimal bias, and support the reliability of the data collected. It is for these reasons that we believe that none of the clinical investigators had disclosable financial interests/arrangements as defined in sections 54.2(a), (b), (c), and (f). The information provided does not raise any questions about the reliability of the data.

Operating Information

Expected Pump Life

The Prometra II programmable pump has a battery which powers the pump. The normal battery life of the pump is a minimum of 10 years at a drug delivery rate of 0.25 mL/day. If you receive a higher flow rate, your battery life may be less. If you receive a lower flow rate, your pump battery should last longer. The below chart will give you an idea of your pump life. If you have any questions, please ask your implanting doctor or pump management doctor.



The only way you can monitor the activity of your Prometra II programmable pump system is by keeping track of how well your symptoms are controlled. Please keep a diary or other daily record of your symptom levels, noting your activities immediately preceding an increase or decrease in symptoms. Set aside time to regularly discuss your daily record with your doctor or refill nurse. Taking an active role in your care will help you to achieve the best symptom control.

Instructions on how to safely dispose of the device

The pump can be removed by your doctor in a surgical procedure like the one that was used to put the pump into your body. Once your pump is explanted, it will be returned to Infusyn Medical for proper disposal.

The pump will need to be explanted upon your death. If you are terminally ill, please notify your caregiver and primary doctor that the pump may explode during cremation and needs to be removed prior to cremation or burial.

Additional Information

Travel or international use

There are no restrictions on travel. However, you will want to arrange with your doctor in advance to obtain the name of a local pump management doctor in case of emergency or prolonged vacation requiring a refill.

Date of Version

August 2024

User Assistance Information

Please contact us with any questions or comments via either phone, email or the web. We always welcome patient input.

- 855.356.9665
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- www.infusyn.com

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