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The alfapump® System Instructions for Use

To be used with Sequana Medical's Smart Charger and **alfa**pump® Programmer IV

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The alfapump® System Instructions for Use

Part of the **alfa**pump® System. Do not combine with other systems. Only to be used with other components of the **alfa**pump® System such as Sequana Medical´s **alfa**pump® and Smart Charger.

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The alfapump® System Instructions for Use

An instructional guide on how to implant the **alfa**pump® System.

Please refer to the **Smart Charger Instructions for Use** for information on charging and the **alfapump® Programmer IV Instructions for Use** for information on programming.

HOW TO USE THIS GUIDE

Information is contained in the following IFUs:

- The **alfapump® System Instructions for Use** gives an overview of the implantable **alfa**pump® System including risks and hazards, contraindications, warnings, precautions and potential interference sources. This guide focuses on describing how to implant and explant the **alfa**pump® System.
- The **Smart Charger Instructions for Use** describes how to use the Smart Charger to charge the **alfa**pump®.
- The **alfapump® Programmer IV Instructions for Use** describes how to use FlowControl Software to adjust **alfa**pump® settings and retrieve pump data stored on the Smart Charger.

The alfapump® System Instructions for Use includes the following:

- System overview including risks and hazards, contraindications, warnings, precautions and potential interference sources
- Implant procedure
- Explant and revision procedures
- Support and service

The **alfa**pump® System, Smart Charger and **alfa**pump® Programmer IV with FlowControl Software must all be used together in order to control the **alfa**pump® and provide optimal therapy for the patient.

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1. The alfapump® System

1.1 Overview

The Automated Low-Flow Ascites Pump (**alfa**pump®) System is an innovative and unique fluid management technology that is designed to improve the lives of patients with refractory ascites. The **alfa**pump® System is a fully implantable, battery powered system which consists of three implantable components: the Peritoneal Catheter SNCA-5262L, the Bladder Catheter and the **alfa**pump®. This system is designed to slowly and continually transport ascites from the peritoneal cavity to the bladder, allowing it to be eliminated from the body through normal urination. The ascitic fluid is transported according to a programmed schedule determined by the physician.

Patient interaction with the system is minimal, requiring only periodic charging of the **alfa**pump® battery through the skin (information on how to charge can be found in the **Smart Charger Instructions for Use**). Each time the patient charges the **alfa**pump®, its pump data is automatically transferred to the Smart Charger. The patient must bring the Smart Charger to each follow-up visit so the physician can transfer its pump data to the provided notebook or tablet (**alfapump® Programmer IV**) for review.

The communication software (FlowControl Software) enables physicians:

- to communicate with the implanted **alfa**pump®,
- adjust the settings based on individual patient needs and
- retrieve pump data via the patient's Smart Charger.

Information on how to use the software can be found in the **alfapump® Programmer IV Instructions for Use**. FlowControl Software comes with the **alfa**pump® Programmer IV provided by Sequana Medical.

1.2 Intended Use

The **alfa**pump® System is intended for single patient use only in adult patients with refractory or recurrent ascites due to liver cirrhosis. It is indicated for the removal of excess peritoneal fluid from the peritoneal cavity into the bladder, where it can be eliminated through normal urination.

Clinicians must be trained by Sequana Medical staff on how to implant and program the **alfa**pump® as well as on how to train the patient to use the Smart Charger.

The patient and/or caregiver must be able to read the Smart Charger Instructions for Use and must be trained by a clinician on how the Smart Charger is used to charge their **alfa**pump®. The Smart Charger with the Docking Station is intended to be used in a home healthcare environment. The Smart Charger with the **alfa**pump® Programmer IV is intended to be used in a hospital environment.

Note: *The **alfa**pump® must be used together with Sequana Medical's Smart Charger and FlowControl Software in order to control the **alfa**pump® and provide optimal therapy for the patient. Please refer to the Smart Charger Instructions for Use and **alfa**pump® Programmer IV Instructions for Use for their respective directions.*

1.3 System Components

alfapump® implantable components

alfapump®

An implantable unit containing a pump, rechargeable battery, associated sensors and electronics.

Peritoneal Catheter SNCA-5262L

An implantable catheter that transports ascitic fluid from the peritoneal cavity to the **alfa**pump®.

Bladder Catheter

An implantable catheter that transports ascitic fluid from the **alfa**pump® to the bladder.

alfapump® implant accessories

Tunneling Rod

A bendable steel rod which is used for tunneling the catheters from the insertion site to the pump pocket.

Bladder Catheter Extension

An additional piece of bladder catheter used for lengthening the tunnelled part of the bladder catheter if required.

Peritoneal Catheter Extension

An additional piece of peritoneal catheter used for lengthening the Peritoneal Catheter SNCA-5262L.

Catheter Extension Connector

A titanium connector used to join two pieces of catheter together.

Introducer Kit

A kit containing several components to introduce the Catheters into the bladder or peritoneal area.

Charging accessories

Smart Charger

A hand-held charger used to charge the **alfa**pump® through the skin, store pump data and wirelessly communicate with the **alfa**pump®. It is also used during implantation.

Docking Station

A base station used to hold the Smart Charger and charge its internal battery. It must always be plugged into a power outlet in order to charge the Smart Charger.

alfapump® Programmer IV and accessories (not required during implantation)

alfapump® Programmer IV with FlowControl Software

alfapump® Programmer IV with FlowControl Software allows physicians to set **alfa**pump® parameters and download **alfa**pump® data via the Smart Charger

Smart Charger USB-C Cable

Connects the Smart Charger to the **alfa**pump® Programmer IV

Medical grade power supply

Connects the **alfa**pump® Programmer IV to the power outlet

Note: *Only components and accessories supplied by Sequana Medical should be used in conjunction with the* ***alfa****pump® System.*

1.4 Device Features

The **alfa**pump® System contains a number of device features to ensure that ascites removal can be performed as intended and be adjusted to meet the needs of each individual patient.

These features include:

- Automated and continual removal of ascites.
- Short and frequent pumping intervals keep the catheters clean and minimize tissue interaction.
- Catheters made of medical-grade silicone with polyester cuffs designed to maintain catheter position.
- Adaptable **alfa**pump® settings to fit individual patient needs.
- Wirelessly programmable by the physician.
- Pressure sensors to monitor the pressure in both the peritoneal cavity and the bladder. The **alfa**pump® can be set to move fluid depending on these pressure levels.
- Multiple mechanisms to ensure that urine cannot pass from the bladder to the peritoneal cavity, minimizing the risk of transmitting infection.
- Rechargeable pump battery– moves approximately 4 liters of fluid per charge.
- The pump can be temporarily turned off if other medical treatments (e.g. intraperitoneal chemotherapy) are performed.

1.5 Risks with Implanting the alfapump® System

Peritoneal cavity infections / Peritonitis

Implantation of the **alfa**pump® System should be postponed until infection resolved if there is an infection in the peritoneal cavity.

Coagulopathy

Ultrasound guided implantation techniques should be considered if there is coagulopathy; the risk of bleeding and arterial puncture needs to be weighed against the potential benefits of the **alfa**pump® System.

Loculated ascites

The presence of loculated ascites prevents the **alfa**pump® System from working efficiently, as it will not be possible to access all areas where the ascites accumulates.

Small bladder capacity and/or obstructive uropathy

Small bladder capacity as well as obstructive uropathy and potential discomfort need to be weighed against the potential benefits of the **alfa**pump® System. A consultation with an urologist is recommended in these situations.

1.6 Medical Therapy Hazards

MRI Safety Information

The **alfa**pump® is MR unsafe.

This diagnostic procedure is contraindicated due to possible movement of the **alfa**pump®, damage to the pump circuitry, tissue damage in the vicinity of the **alfa**pump® and/or catheter dislocation.

Wireless and Data Safety

Wireless communication and data safety between **alfa**pump® and Smart Charger are ensured through a factory pairing mechanism that prevents unauthorized access. Data transferred between the devices is absent from patient demographic and hospital information and is checked for integrity upon every transfer. To avoid data loss backup mechanisms are implemented, this data can be accessed through proprietary software which is available to Sequana Medical only.

Hyperbaric oxygen therapy

Hyperbaric oxygen therapy is contraindicated because the environmental conditions entailed in this therapy are out of the defined range of use for the **alfa**pump® System.

Supersonic therapy and high-frequency heat therapy

Supersonic and high-frequency heat therapies should not be used on patients with the **alfa**pump® System due to possible heating effects of the implanted **alfa**pump®. If the therapy must be performed, it should not be applied in the immediate vicinity of the **alfa**pump® System or the surrounding areas. The **alfa**pump® System should be continuously monitored during the treatment and system function must be checked after the therapy.

Transcutaneous Electrical Nerve Stimulation (TENS)

TENS therapy should not be used on patients with the **alfa**pump® System. If the therapy must be used, the TENS electrodes should be placed as close as possible to each other to reduce the spread of electricity, and as far away as possible from the **alfa**pump®. After stimulation, **alfa**pump® System function must be checked.

Lithotripsy

Lithotripsy should not be used on patients with the **alfa**pump® System because electrical and/or mechanical interferences with the **alfa**pump® are possible. If this therapy must be used, the selected site for electrical and mechanical stress should be as far

as possible from the **alfa**pump®. After the procedure, **alfa**pump® System function must be checked.

Defibrillation

The circuitry of the **alfa**pump® is protected against the energies normally induced by defibrillation. Nevertheless, complete protection is not possible. The implanted **alfa**pump® can be damaged by defibrillation. Circumstances permitting the energy setting should not be higher than necessary for defibrillation and the distance between the paddles and the **alfa**pump® should be at least 10 cm. After defibrillation, the **alfa**pump® System function must be checked.

Radiation therapy

The electronic circuit elements of the **alfa**pump® can be damaged by radiation therapy. The **alfa**pump® should be shielded during the therapy if possible. Following the radiation treatment, the **alfa**pump® System function must be checked.

Electrocautery

Electrocautery should not be performed within 15 cm of an implanted **alfa**pump® because it could damage the pump circuitry. For trans-urethral electro-resection of the prostate, it is recommended to place the neutral electrode on the buttocks or upper thigh, but not in the thoracic area. The **alfa**pump® System function must be checked and monitored after the procedure.

Other implantable medical devices and wearable devices

Other implantable devices such cardiac pacemakers, implantable neuro-stimulators, implantable infusion pumps, implantable infusion pumps circulatory support devices, tachyarrhythmia / implantable defibrillators and cochlear implant systems shall be implanted at least 10 cm from the alfapump. Wearable devices shall also be used at least away 10 cm from the alfapump while charging.

***Note:** Pacemakers, implantable defibrillators and other active implants are not contraindicated but must be verified for proper functioning using manufacturer's labelling after implantation of the **alfa**pump® System.*

1.7 Environmental Hazards

Care has been exercised in the design and manufacture of the **alfa**pump® System to minimize damage under normal use. However, electronic devices are susceptible to many environmental stresses including, but not limited to, the following examples.

1.7.1 Clinical areas Electromagnetic Interference (EMI)

EMI can sometimes cause complications. If complications occur, they will typically be minor and not affect the long-term performance of the **alfa**pump®.

1.7.2 Residential areas Household appliances

Electric household appliances (e.g., stoves, microwave ovens, radios, televisions, VCRs, electric shavers and toothbrushes) will not generally affect **alfa**pump® operation if the appliances are in good condition and properly grounded and insulated.

1.7.3 Mobile phones

Use of mobile phones near the **alfa**pump® during charging and programming has the potential to cause operational complications. Patients should not carry mobile phones in pants pockets or on belt clips within 15 cm of the **alfa**pump®.

Some mobile phones emit signals even when they are not turned on and are only on standby. Potential mobile phone interference while charging or programming is usually temporary and the **alfa**pump® will function properly again once the mobile phone is out of immediate vicinity of the **alfa**pump®.

1.7.4 Interference due to strong electromagnetic fields

Operational complications can be caused by interferences from strong electromagnetic fields, such as those stemming from electric arc welders, electric melting furnaces, radio, radar and television transmitters, exposed ignition systems (e.g., internal combustion engines), electrical tools, high-voltage power lines and defective electrical equipment that is not properly grounded or sufficiently insulated. The patient should seek advice from their clinician before exposing their implanted **alfa**pump® to strong electromagnetic fields.

Note: "*Harmful interference" is defined in 47 CFR §2.1 by the FCC as follows: Interference which endangers the functioning of a radionavigation service or of the other safety services or seriously degrades, obstructs, or repeatedly interrupts a radio communication service operating in accordance with the [ITU] Radio Regulations.*

This device complies with Part 15 of the FCC Rules. Operation is subject to the following two conditions:

(1) This device may not cause interference.

(2) This device must accept any interference, including interference that may cause undesired operation.

1.8 Warnings and Precautions

The following warnings apply to the overall use of the **alfa**pump® System. The techniques and procedures presented in these instructions are not expected to be a substitute for the physician’s experience and discretion in treating any specific patient. Please follow the instructions in this document. Failure to observe these precautions could result in hazardous situations which could result in serious injury.

The **alfa**pump® System and accompanying Smart Charger, Docking Station and **alfa**pump® Programmer IV including FlowControl Software have been tested for compliance with IEC 60601-1 for basic safety and essential performance. All parts of the **alfa**pump® System have been designed for use in the patient environment.

Note: *Changes or modifications to any of the **alfa**pump® System components that are not expressly approved by Sequana Medical could lead to a non-acceptable safety risk to the operator or to the patient unless they are evaluated according to the requirements of IEC 60601-1. Do not modify components of the **alfa**pump® System or combine them with any other components not listed as an accessory to the **alfa**pump® System.*

If there is concern that damage has occurred to any of the **alfa**pump® System components or accessories, or if any component appears to be missing, please contact Sequana Medical's customer service or your local field clinical representative.

General warnings

- Do not disassemble or attempt to repair any of the **alfa**pump® System components.
- Do not attempt to charge other implanted devices like hip implants or pacemakers with the Smart Charger. Do not place the Smart Charger over other implanted devices while charging.
- Only use the provided Docking Station to charge the Smart Charger. Only use the provided power cable to connect the Docking Station to a power outlet. Only use the provided power supply to connect the **alfa**pump® Programmer IV to a power outlet.
- Do not use a multiple socket or extension cord.
- The Docking Station must be plugged into a power outlet while charging the Smart Charger. Docking Station complies with FCC radiation exposure limits set forth for an uncontrolled environment. This equipment (Docking Station) should be installed and operated with a minimum distance of 20 cm between the radiator and the body.
- Do not use the Smart Charger where it may be exposed to flammable gas.
- Do not connect any device to the **alfa**pump® Programmer IV (e.g., an external monitor) other than the Smart Charger (via proprietary USB cable provided by Sequana Medical) or a USB memory stick (to transfer downloaded log files).

Storage and handling

To ensure the **alfa**pump® System operates in accordance with its design specifications, store and handle the **alfa**pump® Programmer IV, Smart Charger and Docking Station with care to avoid damage from environmental factors that may impair their function including, but not limited to, the following:

- Operate the **alfa**pump® Programmer IV, Smart Charger and Docking Station only as intended. Do not use them for any other purpose.

- Do not operate the **alfa**pump® Programmer IV, Smart Charger or Docking Station at an altitude of more than 2000m.
- The **alfa**pump® Programmer IV, Smart Charger and Docking Station are not waterproof. Do not spill water or other liquids on them. If medication or another liquid is spilt on them, wipe it off immediately with a damp cloth.
- Do not use the **alfa**pump® Programmer IV or Docking Station if wet, or connect it to a power outlet with wet hands.
- Recommended storage temperature range is 41°F to 80°F. Extended exposure to temperatures outside this range may result in reduced performance of the **alfa**pump®, Smart Charger or **alfa**pump® Programmer IV due to depleted batteries.
- Store the **alfa**pump® Programmer IV, Smart Charger and Docking Station in a dry place away from direct sunlight.
- Place the **alfa**pump® Programmer IV and Docking Station in a way you can easily access the power cord.
- Keep the **alfa**pump® Programmer IV, Smart Charger and Docking Station out of reach of unsupervised infants and children.

“Use by” date

Check the “use by” date shown on the packages before opening the sterile pack, represented by the icon to the left. Make sure the “use by” date has not expired.

See Appendices A and B for explanations of all symbols used on the device and on the packaging.

Checking sterility

- Prior to shipment, the **alfa**pump®, catheters and accessories are sterilized with ethylene oxide and are packaged for single patient use.
- Before opening the sterile pack, check for any signs of damage that might invalidate the sterility of the contents. If there is any uncertainty about sterility, do not implant that product. Non-sterile products should be returned to Sequana Medical.

Caution: *The device and accessories are protected by double pouches. The inner pouch should only be opened in the sterile field.*

Caution: *Silicone rubber is highly electrostatic and attracts airborne particles and surface contaminants. Exercise care when placing the* ***alfa****pump® and catheters to prevent contact with drapes, lint, dust, surgical glove powder, skin oils, and other surface contaminants. Depositions on the implanted components due to improper handling may cause foreign body reactions.*

Implantation

- The **alfa**pump® and catheters may only be implanted and explanted by a qualified, licensed physician or other authorized healthcare practitioner.
- An appropriate introduction and training must be carried out in advance by a Sequana Medical representative.
- Use proper interventional procedures and sterile techniques.
- Do not use the **alfa**pump®, catheters or any of their accessories if they appear damaged or faulty, or if their packages have been previously opened or damaged. If the package has been pierced or altered, this would render the device or accessory non-sterile.
- Exercise caution when using instruments with the catheters.
- Exercise caution to avoid injury to abdominal viscera and vessels by confirming tip placement before beginning subcutaneous tunneling and by not using excessive force when inserting catheters. For more information on the implant procedure, see section **“2. Implanting the alfapump® System”**.
- Instructions for implanting and explanting the **alfa**pump® System (presented in section **“2. Implanting the alfapump® System”** and section **“3. Explanting the alfapump System”**) are provided for informational purposes only. Each physician should apply these procedures according to his or her professional medical training and experience.
- Non-steroidal anti- inflammatory drugs (NSAIDs) have a marked effect on renal function; therefore, these drugs are to be avoided (for analgesia).
- Drugs that reduce arterial pressure or renal blood flow should be avoided, these include ACE-inhibitors, angiotensin II antagonists, α1-adrenergic receptor blockers.
- Minimize vascular access, no arterial monitoring line, no central venous line, peripheral line only (if possible).
- Liver cirrhosis patients are on a sodium-restricted diet; therefore, volume expansion with solutions high in sodium (such as normal saline) should be avoided.
- The implantation of the alfapump may result in infection that could delay liver transplant or impact transplant listing status.
- The pump rate and potential development of volume depletion of each patient must be monitored by the treating physician to help avoid the onset of acute kidney injury (AKI) and systemic hypoperfusion.
- In order to ensure that the pump can get properly charged, the alfapump shall be implanted at a maximum depth of 3 cm.

Explant and Disposal

- The **alfa**pump® System is for single use only. Do not re-sterilize or re-implant devices that have been explanted.
- Following a complication or failure of treatment, explant or re-intervention may be judged necessary. Explantation and re-interventions will be dependent on the physician‘s judgement and patient‘s wishes. **alfa**pumps® that are explanted for any reason should be returned to Sequana Medical for examination and/or testing. Please contact your Sequana Medical field clinical representative or Sequana Medical at info@sequanamedical.com to arrange for pick-up or shipping.
- In case of patient death, the **alfa**pump® System must be removed prior to burial or cremation. This can be done like by an undertaker, it is not necessarily done by a healthcare professional unless required by local regulations. Depending on local regulations, the removal of battery-operated implantable devices prior to burial is mandatory because of environmental concerns. Please check the local regulations.

***Note**: the cremation process could cause the battery to explode.*

Cybersecurity information

When using the alfapump System, the following needs to be considered to minimize the potential risk of security attacks during use:

- Do not use third party devices with Sequana Medical alfapump System components.

In case of cybersecurity incidents, firmware updates may be performed as part of field safety corrective actions:

- The user is request to comply at its earliest convenience with field safety corrective actions.
- All device corrective actions will be addressed by Sequana Medical personnel.
- Users are not responsible for managing firmware updates themselves.
- In the event of device and cybersecurity concerns, the user should contact Sequana Medical Customer Service (see Customer Service contacts, Chapter 5.1).

1.9 Potential Adverse Events

Potential adverse events (AE) which may be associated with the procedures required to place the device (including the procedure to place the catheters and pump and local and/or general anesthesia) include but are not limited to, the following:

- Adverse reaction to sedation, local or general anesthesia
- Pain
- Sore or irritated abdomen
- Bleeding
- Catheter track bleeding
- Wound dehiscence
- Injuries to the digestive tract during placement
- Injuries to blood vessels
- Abdominal wall haematoma
- Persistent leakage of ascitic fluid
- Peritonitis
- Urinary tract infections
- Cardiac or respiratory arrest connected to underlying medical problems

Potential adverse events (AE) that may be specifically associated with the alfapump® therapy include but are not limited to the following:

- Pump pocket
  - Haematoma
  - Infection
  - Skin erosion above the **alfa**pump®
  - Wound dehiscence
  - Pain
- Surgical
  - Wound dehiscence (rupture)
  - Ascitic fluid leakage
  - Bladder perforation
  - Seroma
- Catheters
  - Kinking
  - Clogging

  - Disconnection from pump
  - Dislocation
  - Migration
  - Infection
  - Tissue damage over catheter trajectory (including erosion)
- **alfa**pump®
  - Erosion
  - Dysfunction
  - Device migration
  - Discomfort during pumping (sensation over the abdomen, filling of the bladder)
  - Externally mediated damage (trauma, radiation)
  - Clogging (prolonged shake mode)
- Infection
  - Peritonitis (abdominal inflammation)
  - Pump pocket
  - Skin
  - Sepsis (including septic shock)
  - Urinary tract
  - Pneumonia
  - Surgical incision
- Reduced kidney function
  - Electrolyte disturbance
  - Acute kidney injury
  - Hepatorenal syndrome
  - Kidney failure
- Genito-urinary complications
  - Hematuria
  - Urethral stenosis
  - Bladder injury
  - Urinary retention
  - Incontinence/leakage
  - Bladder irritation/spasm

- Hepatic encephalopathy
  - Mild-grade I or II
  - Severe-grade III or IV
- Hepatic
  - Progression of liver disease
- Systemic effects
  - Protein loss (hypoalbuminaemia)
  - Circulatory dysfunction (similar to post paracentesis circulatory dysfunction)
  - Dehydration
  - Death

The above risks may require intervention to address the condition.

2. Implanting the alfapump® System

Proper surgical and/or interventional procedures and sterile techniques are the responsibility of the clinical and implant team. The following procedures are provided for informational purposes only; each physician should apply these procedures according to his or her professional medical training and experience.

Clinical considerations

Individual patient anatomy such as obesity, adhesions, weak abdominal wall or loose subcutaneous tissue may require procedural variations.

2.1 Overview

The **alfa**pump® System may be implanted under either local or general anesthesia and typically takes about 60 minutes to 90 minutes. Pre-implant preparation of the patient is essential and includes an examination of abdominal area (see section **“2.3 Patient Preparation”**). The **alfa**pump® is to be placed in a subcutaneous pocket on either the right (preferably) or left side of the abdomen.

The implant procedure includes the following steps:

- Peritoneal Catheter SNCA-5262L placement
- Bladder Catheter placement
- Preparation of the Smart Charger
- Preparation of the **alfa**pump®
  - Waking the **alfa**pump®
  - Priming the **alfa**pump®
- Pump pocket creation and catheter tunneling
- Connecting the catheters to the **alfa**pump®
- Testing the **alfa**pump®
- Closing the incisions

2.2 Implant Kit Components and Procedural Tools

Components shipped as part of the alfapump® System

Within each implant kit are 6 boxes and one charging kit. Each of the 6 boxes includes a multi-language product information sheet with specific product information. Each sterile component included in the **alfa**pump® System is individually packaged in a pouch or blister tray and labeled. Each package should be inspected for potential damage prior to opening. If the packaging is damaged, discard and use another **alfa**pump® System.

Contact Sequana Medical's customer service or local field clinical representative if damage to the package is discovered prior to the scheduled implant so a replacement can be provided.

Each **alfa**pump System includes the following:

- **alfa**pump® System Instructions for Use
- Smart Charger Instructions for Use
- **alfa**pump®
  - Catheter Locking Cap
  - Priming Tube
- Bladder Catheter
  - Blunt stylet
- Peritoneal Catheter SNCA-5262L
- Tunneling Rod
- Implant Accessories
  - Catheter Extension Connector
  - Bladder Catheter Extension
  - Peritoneal Catheter Extension
  - Catheter Locking Cap
- Introducer Kit (two)
  - 18 Fr Peel-Away introducer sheaths (with dilator inserted)
  - 14Fr dilator
  - 10 Fr dilator
  - 0.038" double-ended guidewire (a "J"-shaped and a straight end)
  - 18 gauge puncture needle stored in a sleeve
- Smart Charger Carrying Case
  - Smart Charger
  - Docking Station
  - Power cord
  - Smart Charger Instructions for Use

Procedural tools required for implantation:

In addition to the components provided by Sequana Medical listed above, each implant procedure will also require the following:

- 5 cc to 10 cc syringe
- Sterile medical grade lubricant or ultrasound gel
- Optional
  - Skin marker
  - Medical grade dye e.g. methylene blue or radiological contrast fluid

2.3 Pre-Implant Patient Preparation

- Perform an abdominal ultrasound examination to assess omentum free space.
- Paracentesis 1 day prior to scheduled surgery to reduce tension and check for infection. Drain the patient of ascites but leave approximately 0.5L of ascites so there is enough fluid for placement of the peritoneal catheter. Provide, Albumin infusion according to your local guidelines.
- Initiate an i.v. prophylactic broad spectrum antibiotic cover 24 hours pre-operatively and maintain for at least 24 hours post-operatively, then change to per os.
- Insert a Foley catheter, drain the bladder, then load the bladder with up to 500 ml sterile saline. Consider to add methylene blue as aid to confirm correct bladder catheter placement. Clamp the Foley catheter. Consider insertion after sedation to reduce patient discomfort and anxiety.

2.4 Procedure Preparation

Make sure all components and tools listed above in section **“2.2 Implant Kit Components and Procedural Tools”** are available. Additionally, make sure to have a back-up system available so components are available in case their use is deemed necessary.

Prepare surgical sites and sterile drapes as per standard operating practice.

2.5 Catheter Insertion

***Note**: Exercise care when placing the peritoneal and bladder catheters to prevent them from coming into contact with surfaces such as drapes or towels. Silicone rubber is highly electrostatic and attracts airborne particles and surface contaminants.*

***Note**: When clamping the Peritoneal Catheter SNCA-5262L or Bladder Catheter always use a clamp with non-serrated jaws or use a rubber-shod instrument.*

Peritoneal Catheter SNCA-5262L placement

1. Locate the insertion site through which to place the Peritoneal Catheter SNCA-5262L. The catheter insertion site is typically near the right pericolic gutter. Use Doppler ultrasound to avoid any large vessels. Insertion site needs to be individualized per patient's anatomy so that the subcutaneous path of the peritoneal catheter is at least 10 cm from the peritoneal catheter incision site to the pocket. A minimum distance of 10cm is recommended though this might not always be feasible due to patient dimensions and anatomical characteristics. If the minimal advised tunnel length is not feasible, extra attention to closure of the double purse string suture is warranted.
2. Take care that the incision site does not sit directly below pressure points e.g. trouser belt.

   - Cut the Peritoneal Catheter SNCA-5262L between the two cuffs, past the bend and close to the second cuff, attach the Catheter Extension Connector and Peritoneal Extension Catheter (blue extension tube). Fixate the catheters to the connector using sutures.
   - Create an incision through the skin of approximately 2-3 cm in order to allow for a double purse string suture.
   - Using the puncture needle, puncture the peritoneal cavity and then check whether fluid can be aspirated.

   Note: *To provide additional stabilization during puncturing and to facilitate the monitoring of reflux, a syringe may be added to the puncture needle.*

   - If a syringe has been used, remove it from the puncture needle while keeping the needle in place and cover the end with place the thumb / finger on the outer puncture needle end to prevent fluid leakage
   - Hold the puncture needle in position and slowly insert the guidewire through the puncture needle until it reaches the desired position (approximately half way).

   Note: *To insert the "J"-shaped end of the guidewire, it is recommended to use the supplied insertion aid to insert it into the puncture needle.*

   Caution: *Do not advance the guidewire if it encounters resistance; In this case, the puncture needle should be withdrawn a little and then try again to move the guidewire forward.*

   - While holding the guidewire, slowly remove the puncture needle.
   - Insert the 10 Fr dilator over the guidewire and then pull it back.
   - Insert the 14 Fr dilator over the guidewire and then pull it back.
   - Insert the 18 Fr Peel-Away introducer sheath (with dilator) over the guidewire.
   - Remove the guidewire from the Peel-Away introducer.

- Release the dilator from the Peel-Away introducer sheath by turning the dilator about 90° counterclockwise. Then pull the loosened dilator out of the Peel Away introducer sheath. Then place your thumb / finger on the opening to prevent fluid leakage.
- Lubricate the insertion rod and the outside of the catheter with medical biocompatible lubrication gel.
- Insert the Bladder Catheter Blunt Stylet into Peritoneal Catheter SNCA-5262L and introduce catheter through the peel- away introducer as far as the catheter cuff.
- Split the sheath by pulling the tabs on either side. Pull the sheath apart while sliding the catheter down over the stylet until the cuff is positioned at skin level.
- Remove the stylet and verify free flow of ascitic fluid. Do not remove all ascitic fluid prior to pump testing.
- A double purse string suture through the fascia should be used to reduce the chance of leakage. This will position the cuff as close to the fascia as possible and lay flat under the skin to avoid pressure on the subcutaneous part of the skin.

Bladder Catheter placement

1. Assess the bladder with ultrasound.
   - Locate the incision site above the symphysis pubis and below the palpable bladder dome.
   - The incision site should be right to the midline.
   - Perform a bladder “stab” with the puncture needle attached to a small syringe whilst aspirating. Confirm the correct placement by free aspiration of urine/ saline/dye (colored if methylene blue was used). Alternatively, inject contrast medium via the needle to confirm correct bladder access.
2. Lubricate the insertion rod and the outside of the catheter with medical biocompatible lubrication gel.
3. Pull the proximal fitting on the tubing toward the luer fitting on the insertion rod until the tip of the rod completely straightens the coil and the tip of the rod is visible at the end of the catheter.
4. Ultrasound visualisation of the bladder size and position may be useful during the bladder “stab” especially in obese patients or those with “over-hanging” ascites.
5. Remove the syringe from the needle then insert the guidewire through the needle into the bladder.

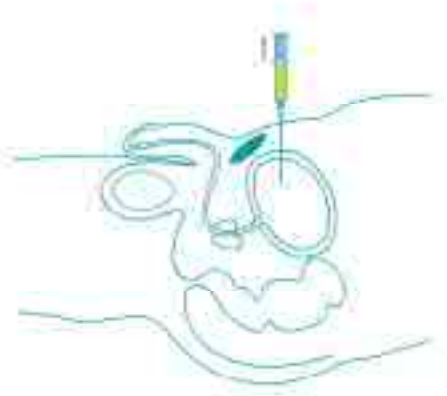


Figure 2-1: Remove syringe

Figure 2-2: Insert guidewire

Note: *To insert the "J"-shaped end of the guidewire, it is recommended to use the supplied insertion aid to insert it into the puncture needle.*

Caution: *Do not advance the guidewire if it encounters resistance; In this case, the puncture needle should be withdrawn a little and then try again to move the guidewire forward.*

6. While holding the guidewire, slowly remove the puncture needle.
7. Insert the 10 Fr dilator over the guidewire and then pull it back.

   Note: *Do not insert the dilator too far, otherwise the posterior bladder wall may be damaged.*
8. Insert the 14 Fr dilator over the guidewire and then pull it back.

   Note: *Do not insert the dilator too far, otherwise the posterior bladder wall may be damaged.*
9. Insert the 18 Fr Peel-Away introducer sheath (with dilator inserted) over the guidewire.

   Note: *do not insert the Peel-Away introducer sheath (with dilator inserted) too far, otherwise the posterior bladder wall may be damaged.*
10. Remove the guidewire from the Peel-Away introducer.
11. Release the dilator from the Peel-Away introducer sheath by turning the dilator about 90° counterclockwise. Then pull the loosened dilator out of the Peel Away introducer sheath. Then place your thumb / finger on the opening to avoid fluid leakage

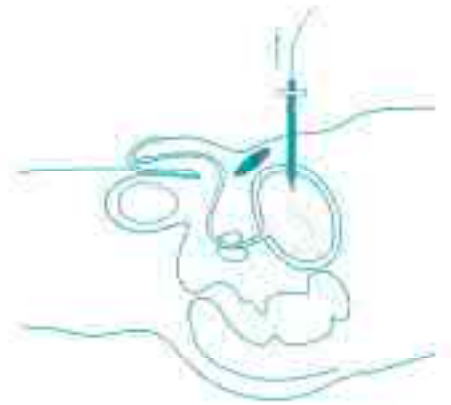


Figure 2-3: Remove dilator and guidewire

12. Introduce the Bladder Catheter through the peel-away introducer.

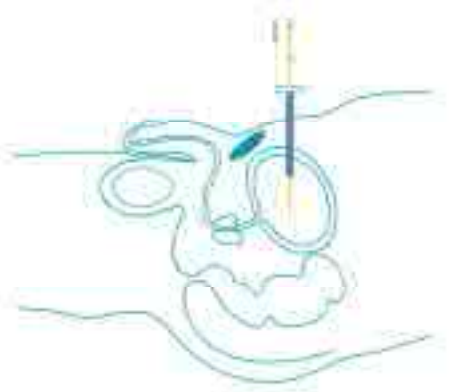


Figure 2-4: Bladder Catheter introduction

13. Slide the Bladder Catheter down along the rod until the cuff is touching the top of the introducer. Split the sheath by pulling the tabs on either side. Pull the sheath apart while continuing to slide the catheter down over the rod until the cuff is positioned below skin level.
14. Remove both the peel-away introducer and the rod, making sure the Bladder Catheter stays in place. Ensure that the coil resides completely in the bladder.
15. Allow the bladder to drain to verify correct placement.
16. Using non-resorbable sutures, create an anchor point around the felt cuff of the tubing to prevent catheter migration. The sutures should be tied into stable tissue that can support occasional force from catheter movement such as the Suprapubic Aponeurosis. It is important that the sutures are tight enough to secure the catheter but not tight enough to collapse the lumen or cut into the tubing.
17. Cut the tubing next to the fitting on the catheter tubing and remove the fitting.
18. Clamp the Bladder Catheter.

2.6 Using the Smart Charger during implant Procedure

To prepare the **alfa**pump, its corresponding Smart Charger is required. Smart Charger features are as follows:

1 Display

2 On/Off button

3 Power connectors

4 USB connectors

5 Multifunction button

6 Charging lights (visible when charging)

7 Charging coil

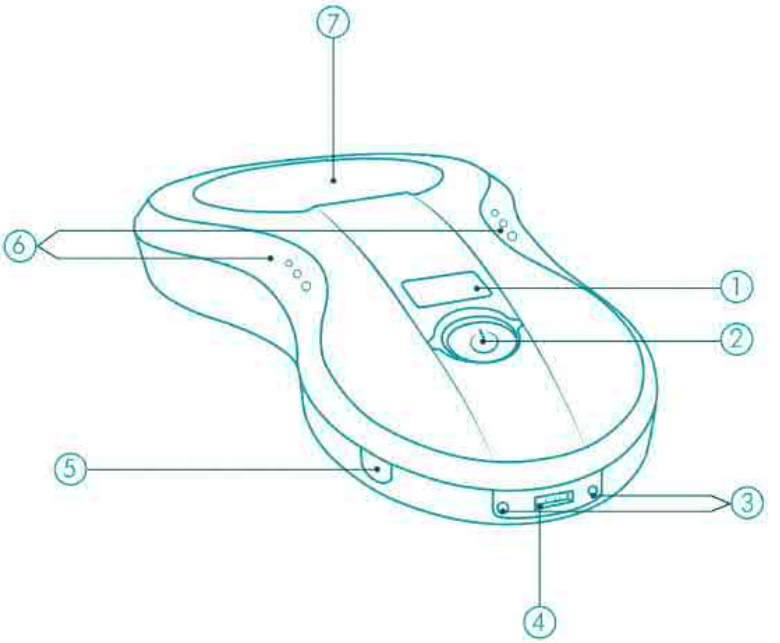


Figure 2-5: Smart Charger features

On/Off button

The On/Off button is used to start and stop charging of the implanted **alfa**pump® once the charger has been positioned. Charging the **alfa**pump® initiates communication between **alfa**pump and FlowControl Software when the proprietary USB cable is connected.

Charging coil

The charging coil sends out the power to charge the **alfa**pump®. The charging coil should always be placed as close as possible to the implanted **alfa**pump®.

Charging indicators

When illuminated, the charging indicators are visible from both sides of the Smart Charger and shine green, yellow or red.

Display

The display provides you with information on the battery and the charging status. When the Smart Charger is not charging the **alfa**pump®, this display will show the battery status of the Smart Charger.

While charging of the **alfa**pump®, this display will show either the battery status of the implanted **alfa**pump® or an indication of charger and pump contact to help you maximize the charging. If an error occurs, the charger will inform you of this by displaying an error icon (see section **"2.7 Preparing the Smart Charger"** for explanations on error icons).

Multifunction button

The multifunction button allows you to toggle between the different messages on the display. As long as the prime pump mode is enabled, the multifunction button allows you to test the paired **alfa**pump® (once communication is established).

Power connector

At the side of the Smart Charger there are two power connectors which connect to the two pins on the Docking Station.

USB connector (only to be used by the physician)

At the side of the Smart Charger there is a socket where a USB cable can be inserted. This may only be used by the physician, who has a special USB cable which allows downloading of pump data.

While the implanted **alfa**pump® is being charged, the pump data is transferred automatically to the Smart Charger. This means that when the patient's Smart Charger is connected to the **alfa**pump® Programmer IV, all pump data will be accessible, right up until the last time the **alfa**pump® was charged.

Caution: *DO NOT put the Smart Charger on metal surfaces or near any other electronic equipment or credit cards when charging.*

2.7 Preparing the Smart Charger

The Smart Charger has been switched off for shipment and storage and must be switched back on prior to implanting the **alfa**pump. You can switch on the Smart Charger by firmly pressing the multifunction button.

Alternatively, connect the Docking Station to a power outlet and place the Smart Charger firmly into the Docking Station. The Smart Charger will wake up and display the Sequana Medical logo together with the serial number of the Smart Charger and other information. Ensure that the **alfa**pump®'s serial number shown on the bottom line of the display corresponds to the serial number of the **alfa**pump® you are about to implant.

Once you have verified that these numbers match, press the On/Off button to continue. Make sure the Smart Charger is still sitting in the Docking Station. The Smart Charger

will begin charging; verify that the battery of the Smart Charger is above 50% by checking the display.

2.8 Preparing the alfapump®

Prior to unpacking the **alfa**pump® in the sterile field, activate ("wake") the **alfa**pump® by initiating a manual pump cycle.

To wake the alfapump:

1. Place the Smart Charger over the **alfa**pump® (still in its sterile pouch) and turn on the Smart Charger by pressing the On/Off button. The Smart Charger will beep and the yellow charging indicators will illuminate. On the screen the message, pump priming enabled' will appear (see **"Table 2-1: Warning Messages"**).
2. Move the Smart Charger in order to find the optimal position until you see at least one yellow bar (see Figure below).

*Figure 2-6: Good quality of charging the **alfa**pump®*

3. Wait until the Smart Charger's display shows the **alfa**pump®'s battery charge level. This indicates communication with the **alfa**pump®.

*Figure 2-7: Communication with **alfa**pump® established*

***Note:** In rare cases it can happen that the **alfa**pump® is not starting to communicate. You will then need to turn off the Smart Charger and wait for at least five minutes to give the **alfa**pump® time to reset its communication.*

4. While charging the **alfa**pump® press the multifunction button to enter the manual pump mode. The display will indicate the quality of radio communication between the Smart Charger and the **alfa**pump® (see Figure below). The longer the bar, the better the reception is.

*Figure 2-8: Good quality of radio communication to the **alfa**pump®*

5. The **alfa**pump® is now awake and ready to be primed.

6. If you have communication you may press the On/Off button. The display will switch to pump mode and the **alfa**pump® will start a pump cycle. After the pump cycle has finished, the result of the pump cycle will show on the Smart Charger's display. Verify that you see a green 'OK' sign.

Figure 2-9: Green 'OK' sign, yellow 'warning' sign and red 'error' sign

7. When you have verified that the green 'OK' sign appears press the On/Off button again to display the quality of radio communication, you are ready for a new cycle. Do not leave the self-prime mode until the implantation is finished. This mode is also used to test the pump and catheters during the procedure.

8. When communication is lost, you will see the following screen and the yellow charging indicators will flash. Move closer to the **alfa**pump® until the red bar disappears. If you are not able to re-establish communication with the **alfa**pump® within five minutes, you will need to repeat the steps listed above to wake the **alfa**pump® again. For this, you will need to place the Smart Charger in a sterile bag because the Smart Charger is provided non-sterile.

*Figure 2-10: Poor quality of radio communication to the **alfa**pump®*

***Caution:** Communication between the Smart Charger and **alfa**pump® will stop after 60 minutes of non-communication while the prime mode is active and 5 minutes after the prime mode is disabled.*

***Note:** Once the **alfa**pump® is activated, it can be unpacked and handed over to the surgical team. The next step is to confirm the **alfa**pump® is primed by performing a manual pump cycle while the **alfa**pump® is submerged in sterile saline.*

To prime the alfapump®:

1. Remove the yellow priming tube from between the two nipples and connect it to the nipple closest to the text side of the pump, which is on top when placed in the packaging tray.

2. Connect a syringe to the other end of the yellow tube and place the **alfa**pump® back in the packaging tray.

3. Fill the tray with sterile saline and ensure the other nipple is fully submerged.

Note: *Using another container may lead to poor communication between the Smart Charger and the* ***alfa****pump®, impairing the manual pump mode.*

4. Gently pull on the syringe to aspirate air out of the **alfa**pump®. Keep pulling until saline enters the syringe.

   Note: *Do not try to push saline through the* ***alfa****pump® as this may damage the* ***alfa****pump®. If saline is pushed inside the* ***alfa****pump®, please use another* ***alfa****pump®.*

5. Prime the **alfa**pump® again using the Smart Charger and verify that you see a green 'OK' sign.

6. The **alfa**pump® is now successfully primed. Remove the yellow tube.

Note: *If priming is still unsuccessful as observed by lack of fluid exiting from the yellow tube, please use another* ***alfa****pump® and Smart Charger.*

2.9 Pump Pocket Creation and Catheter Tunneling

1. Make a transversal incision 6 cm to 7 cm in length beneath the costal margin. The exact location where to create the pump pocket should be identified based on patient characteristics, location of the peritoneal catheter incisions site, catheter tunnel path, and can be influenced by anatomical landmarks (e.g. the presence of a (umbilical) hernia or scars from previous interventions) or and by patient condition (sufficient subcutaneous tissue in patients with sarcopenia).

   Note: *The distance from the Peritoneal Catheter SNCA-5262L insertion point to the pump pocket should preferably be at least 10 cm.*

2. Using blunt dissection, create the pump pocket (it may be useful to use the **alfa**pump® as a template to create the pocket). The pump should be implanted above the abdominal wall fascia.

   Note: *the* **alfa***pump shall be implanted at a maximum depth of 3 cm.*

3. The pump pocket must be large enough so now sharp contours are visible.

4. The pump should be implanted outside the peritoneal cavity.

5. Insert the tunneling rod subcutaneously into the catheter incision site and attach the catheter, tunnel the catheter following the fascia according to the pre-specified path (avoiding any vessels and stay subcutaneously) to the upper right corner of the pump pocket. Ensure the catheters lay flat under the skin avoiding any pressure points. If started with the PC, repeat this process for the BC.

Figure 2-11: Push the loose end of the catheters firmly onto the Tunneling Rod

Caution: *It is important that a clamp or hemostat is not used to pull the catheters through, as this will create a large channel through which ascitic fluid may leak.*

6. Verify the function of each catheter by injecting and aspirating fluid through each catheter using a syringe. If fluid is present in the abdomen/bladder, fluid should flow spontaneously from the catheters.

7. Using the **alfa**pump® as a guide, trim the length of the bladder and peritoneal catheters to fit. Make sure to allow sufficient slack to slide the **alfa**pump® into the pocket and for normal movement of the upper body, but not too much as it can lead to “kinking”.

   Note: *If more catheter length is needed, attach the Bladder Batheter Extension to the Bladder Cather using the Catheter Extension Connector (all provided with the Implant Accessories). After connecting the tubing onto the Catheter Extension Connector, securely tie a loop of non- resorbable suture around each end to lock the tubing onto the fitting.*

Figure 2-12: Tubing suture

8. Insert the trimmed ends of the catheters into the CatheterLocking Cap (the yellow, round Bladder Catheter through the round hole; the blue, square Peritoneal Catheter Extension through the square hole).

9. Push the catheters fully onto the **alfa**pump® nipples using the Catheter Locking Cap to determine correct orientation. Before securing the Catheter Locking Cap into place on the **alfa**pump®, test the **alfa**pump® (see section **“2.10 Testing the alfapump® ” on page 39**”).

   Note: *Please push the catheters carefully on the nipples avoiding pinching the catheters with a sharp tool. Damaging the catheters may lead to leakage inside the pump pocket.*

10. Lock the catheters in place with the Catheter Locking Cap. For this, push the Catheter Locking Cap firmly unto the pump until you feel the little hook settling into place. Eventually you need to pull slightly on the two catheters to avoid them bunching up.

    Caution: *Once the catheters and Catheter Locking Cap are connected to the **alfa**pump®, they are difficult to remove. Ensure proper catheter placement and length prior to connecting the Catheter Locking Cap to the **alfa**pump®. If the catheters have to be detached from **alfa**pump®, pull strongly on the catheters to remove both of them before removing the Catheter Locking Cap.*

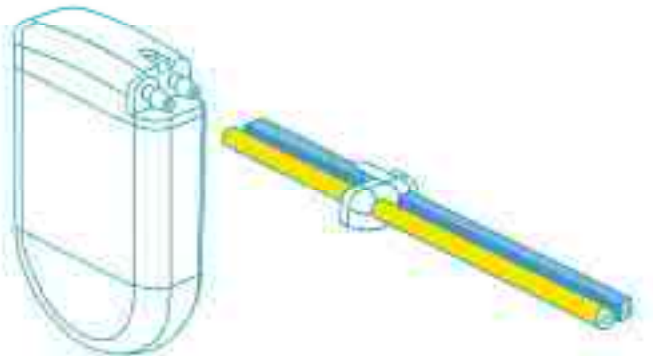


Figure 2-13: Catheter Locking Cap placement on catheters

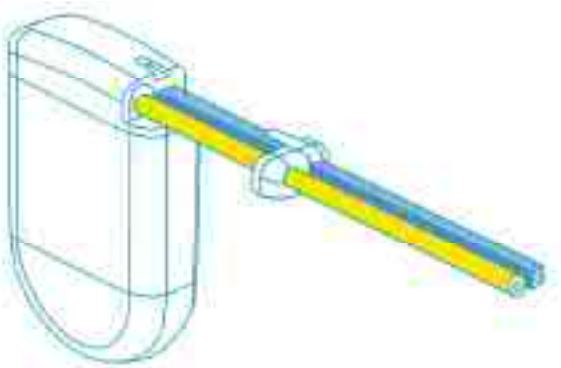


Figure 2-14: Connect catheters firmly to ***alfa****pump nipples*

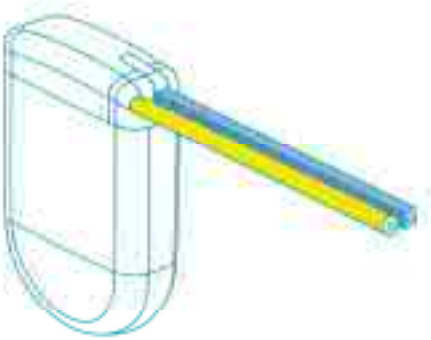


Figure 2-15: Push Catheter Locking Cap onto the pump until you feel the little hook settling in place

11. Slide the **alfa**pump® into the pump pocket and verify the catheters are not kinked or bent.

    Caution: *The felt pads on the* ***alfa****pump® must face internally to allow for charging.*

12. Place subcutaneous sutures deep into the pocket and through the **alfa**pump®'s fixation holes. This keeps the **alfa**pump® firmly in the base of the pocket and prevents migration of the **alfa**pump® towards the incision.

2.10 Testing the alfapump®

When connecting the catheters to the **alfa**pump®, before locking the Catheter Locking Cap, you must run a manual pump cycle to ensure good functionality of the **alfa**pump®.

1. Verify that the Smart Charger is still communicating with the **alfa**pump® by looking at the Smart Charger's display. There should be a bar representing the communication level, see Figure below.

*Figure 2-16: Perfect quality of radio communication to the **alfa**pump®*

***Note:** Communication between the Smart Charger and **alfa**pump® will stop after 60 minutes of non-communication while the prime mode is active and 5 minutes after the prime mode is disabled. If communication is lost, the following screen is displayed and the yellow charging indicators will flash:*

*Figure 2-17: No radio communication to the **alfa**pump®*

2. Move closer to the **alfa**pump® until the red bar disappears. If you are not able to re-establish communication with the **alfa**pump® within five minutes, you will need to repeat the steps in section **"2.8 Preparing the alfapump®"** to wake the **alfa**pump® again. Place the Smart Charger in a sterile bag because the Smart Charger is not provided sterile.
3. Press the On/Off button on the Smart Charger. The **alfa**pump® will start a pump cycle. After the pump cycle has finished, the result of the pump cycle is shown on the Smart Charger's display. Verify that a green 'ok' sign is displayed.
4. If a yellow warning sign is displayed instead, the pump incurred a dropdown. This means that the pump was not able to pump fluid either because the Peritoneal Catheter SNCA-5262L was kinked or because there was no fluid at the location of the Peritoneal Catheter SNCA-5262L. Try to reposition the Peritoneal Catheter SNCA-5262L and perform another manual pump cycle until the green 'ok' sign is displayed.

   ***Note:** If a red 'error' sign is displayed instead of the green 'ok' sign, please use another **alfa**pump® and Smart Charger.*

2.11 Closing Incisions

- Perform a multi-layer water-tight closure of the pump pocket, ensuring that neither the **alfa**pump® nor the catheters cross the line of the initial incision.
- Perform a multi-layer closure of the Bladder Catheter implantation site incision.
- Perform a multi-layer closure of the Peritoneal Catheter SNCA-5262L implantation site incision.
- To disable manual pump cycles, press the On/Off button and the multifunction button simultaneously. Alternatively, enable fluid transport using FlowControl Software/FlowTech Software which will automatically disable the prime mode.

2.12 Patient care post implant

- It is recommended to start the pump directly post implant at 120% of the estimated rate of ascites production and will be fine-tuned postoperatively. Patients should leave the OR with less than one liter of ascites. Replace Albumin eas needed.
- For patient comfort, it is recommended to leave the Foley catheter in place for the first 24 hours post implant.
- Pump charging will start on the ward and patients should be trained in the use of the SmartCharger at the same day as the operation and repeated during initial hospitalization.
- Postoperative albumin replacement is recommended if more than three liters of ascites is drained during the implant procedure.
- NSAIDs have a marked effect on renal function; therefore, non-steroidal anti-inflammatory drugs for analgesia are to be avoided.
- Drugs that reduce arterial pressure or renal blood flow should be avoided.
- ACE-inhibitors, angiotensin II antagonists, α1-adrenergic receptor blockers should be avoided.
- Minimize vascular access, no arterial monitoring line, no central venous line, peripheral line only (if possible).
- Liver cirrhosis patients are on a sodium-restricted diet; therefore, volume expansion with solutions high in sodium (such as normal saline) should be avoided.
- Take dietary restrictions into account while the patient is hospitalized.
- Careful monitoring of and attention to wound care post implant and patient education on wound care is essential to minimize risk of implant site infection. It is recommended that the stitches remain in site for at least 2 weeks.

- In case of postoperative infection and wound erosion, conservative treatment with antibiotics should commence unless the patient is septic or when the pump is visible through the wound, the pump should be explanted.
- Post-suprapubic catheterization insertion, there should be a high index of suspicion for bowel perforation if the patient has abdominal pain or is otherwise unwell and presents features of localized peritonitis.

2.13 Returning Non-Used Devices

Please return any devices to Sequana Medical which were opened but not implanted (**alfa**pump, Smart Charger or catheters). Please contact Sequana Medical's customer service or local field clinical representative to arrange this.

2.14 Activating and Programming the alfapump®

Please refer to the **alfa**pump® Programmer IV Instructions for Useprior to using FlowControl Software.

Activation of the pump at appropriate volumes during the implantation procedure is recommended to avoid fluid accumulation and associated fluid leakage from the early post-implant skin and subcutaneous defects.

2.15 Warning and Error Messages

The Smart Charger ensures patient safety. If there is any warning or error, the Smart Charger will stop charging the **alfa**pump® sound two short beeps and show one of the following messages:

Table 2-1: Warning Messages

Message	What it means	What to do
	A timeout has occurred. The Smart Charger has been using its maximum allowed power	Turn off the Smart Charger and wait 10 minutes before charging again.
	A timeout has occurred. The Smart Charger has not been communicating with the **alfa**pump®.	Turn off the Smart Charger and wait 10 minutes before charging again.
	A timeout has occurred. The Smart Charger has not been charging the **alfa**pump®.	Turn off the Smart Charger and wait 10 minutes before charging again.

	The **alfa**pump® has become too hot and the Smart Charger has stopped charging.	Turn off the Smart Charger and wait 10 minutes before charging again.
	A timeout has occurred, self-priming was active for more than its allowed time.	If you have finished the implantation just turn off the Smart Charger. If you are still implanting reactivate self- prime mode within 2 minutes (the pump should still communicate)
	The Smart Charger is defective, but limited charging is still possible.	Contact Sequana Medical to arrange for a replacement.
	The **alfa**pump® manual pump mode has not been turned off.	Please turn off manual pump mode prior to handing the Smart Charger to the patient. Refer to section **“2.16 Patient Care”** for instructions.
	The calibration of the Smart Charger is not valid	Contact Sequana Medical to arrange for a replacement
	The **alfa**pump® manual pump mode has successfully been turned off.	There is nothing to do.
	The Smart Charger has been reset.	Press the On/Off button to continue.

Table 2-2: Error Messages

Message	What it means	What to do
	The Smart Charger is using too much power.	Turn off the Smart Charger and move it away from any metal surfaces; wait 10 min-utes before charging again.
	The temperature of the Smart Charger is too high.	Turn off the Smart Charger and wait 10 minutes before charging again.

	The Smart Charger is receiving conflicting information from the **alfa**pump®.	Turn off the Smart Charger; be sure no other patient is in the same room and start charging again.
	The Smart Charger may have malfunctioned.	Exchange the Smart Charger and contact Sequana Medical to pair it to the **alfa**pump®.
	Error code displayed while using the Smart Charger.	Contact Sequana Medical and report code.

2.16 Patient Care

Please ensure that the patient receives the Smart Charger paired to the implanted **alfa**pump®.

Note: *Please ensure that the prime mode is disabled prior to giving the Smart Charger to the patient. To do this, turn on the Smart charger, start charging (no pump required) and wait until the display shows that the Smart charger is searching for the pump. Press and hold the multi-function button while keeping the multi-function button held down, press the On/Off button. This will switch off the Smart Charger and disable the prime mode. You will see a confirmation display as depicted in* ***Table 2-1: "Warning Messages"****.*

- **alfa**pump® parameters should be set either the same day of implantation (a few hours later) or the day after. The physician also needs to verify the function of the **alfa**pump®.
- The patient must be trained on how to use the Smart Charger. Make sure he or she is in possession of the Smart Charger, Docking Station and Smart Charger Instructions for Use.
- Regular visits should be scheduled to check the **alfa**pump® and ensure optimal therapy.

For further information on how to program the **alfa**pump® and how to adjust the settings of the **alfa**pump®, please consult the **alfapump® Programmer IV Instructions for Use**.

3. Explanting the alfapump® System

The **alfa**pump® System is designed for long-term implantation. Explantation of the entire system can be required in specific conditions such as infection, lack of efficacy or reduction of symptoms after receiving a new liver or any circumstance in which the patient is no longer producing (significant) amounts of ascites. The **alfa**pump® System should also be explanted after patient death. This section details the procedure in which the alfapump is explanted or revised in patients that have not died.

Prior to explantation, please ensure that the patient's physician has switched off the **alfa**pump® using FlowControl Software. For details on how to switch off the **alfa**pump® please refer to the **alfapump® Programmer IV Instructions for Use**.

3.1 Patient Preparation

The **alfa**pump® System may be explanted under either local or general anesthesia. The patient should have a bladder catheter (e.g Foley catheter) for at least 24 hours after the procedure. The Foley is needed to ensure that no urine will leak in the abdominal cavity and the hole of the supra-pubic bladder catheter will close. Prophylactic antibotics should be administered to prevent infection.

3.2 alfapump® Removal

1. Open the pump pocket via an incision of the skin.
2. Cut the sutures that fixed the **alfa**pump®.
3. Remove the **alfa**pump® from the pocket. Note, due to tissue growth into the felt discs on the posterior surface of the pump, removal will be difficult and dissection of the tissue from the felt discs will be required.
4. Make an incision in the supra-pubic area at the initial incision used for Bladder Catheter implantation.
5. Locate the Bladder Catheter and fixation suture.
6. Cut the fixation suture and ensure all suture material is removed.
7. Locate the felt cuff and ensure it is freed from tissue.
8. Cut the Bladder Catheter and pull the distal part out of the bladder.
9. Cut the Bladder Catheter at the **alfa**pump® side and pull the tubing out via the supra-pubic incision.
10. Make an incision at the location of the initial implantation for the Peritoneal Catheter SNCA-5262L and locate the felt cuff.
11. Cut the fixation suture (if sutured) and ensure all suture material is removed.

12. Ensure the felt cuff is freed of surrounding tissue.
13. Cut the tubing and pull out the tubing from the peritoneal cavity.
14. Cut the tubing at the **alfa**pump® side and pull out the tubing via the peritoneal catheter incision.
15. Remove the **alfa**pump® and close all incisions.

Note: *Please make sure that all components are explanted.*

3.3 Revision Procedures

For any revision procedure it is important that the **alfa**pump® is fully charged even if the pump was not performing during the last months. If the pump function cannot be fully verified during a revision it is advisable to exchange the pump.

Note: *Please instruct the patient to charge his or her **alfa**pump® prior to a revision.*

Most revisions may be performed using local anesthesia with, where necessary, some sedation. Note that pump replacement after some weeks of implantation will be difficult due to tissue growth into the felt anchoring discs. In this instance sedation is recommended.

Exchange of catheter

If a catheter is blocked or dislocated, a partial revision can take place. For this, only the initial catheter incision needs to be opened. A new catheter should be placed, after which the distal part of the old catheter can be cut off and removed. The tubing can be reconnected with the Catheter Extension Connector provided by Sequana Medical. After connecting the tubing onto the Catheter Extension Connector, securely tie a non-resorbable suture around the tubing to secure in place.

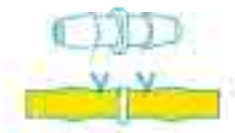


Figure 3-1: Tubing suture

Exchange of alfapump®

If the **alfa**pump® needs to be exchanged, the pump pocket should be opened and the fixation suture removed. The catheters should be pulled, with some force, from the **alfa**pump®. After fixing the new **alfa**pump®, the incision should be closed.

Make sure that the **alfa**pump® is either re-programmed to work with the original Smart Charger or exchange the Smart Charger as well so that it is paired with the new **alfa**pump®.

4. Summary of Clinical Study Results

Introduction

This report describes the results of the primary endpoint analysis through 6 months as well as other endpoints through and post 6 months of the study entitled "***alfa****pump*® *System in the treatment of refractory or recurrent ascites: a multicenter single arm within subject crossover design pivotal study*", the POSEIDON Study. Sequana Medical, who is the sponsor of this study, developed the **alfa**pump® System to improve the lives of patients with refractory or recurrent ascites by slowly and continually transporting ascites from the peritoneal cavity to the bladder, allowing it to be eliminated from the body through normal urination. The study is being conducted in the US and Canada. All patients have completed the Primary Endpoint and the 12-month follow-up endpoint. The study is currently continuing in the post 1 year follow-up phase. Patients are being followed through 24 months follow-up post-implant and may enter an optional long-term follow up period for continued evaluation between 2 and 5 years.

NOTE: This study report reflects the data that was available until the data cut on 01 November 2023. Data through 24 months and optional long-term follow-up is therefore not yet complete and subject to change.

Objectives

The objective of the clinical investigation is to assess the clinical safety and effectiveness of the **alfa**pump® System in removing ascitic fluid from the peritoneal cavity in cirrhotic liver patients with refractory or recurrent ascites. More specifically, the study was designed to collect and analyze data to assess:

• The effectiveness of the alfapump in controlling ascites as determined by the reduction in the need for repeated paracentesis compared to baseline.

• The safety of the alfapump implant procedure and alfapump therapy as determined by the rate of explants, reinterventions, and other serious device or procedure related adverse events.

• Patient-reported outcomes (assessed by SF-36 Physical Component Score as well as a disease-specific validated questionnaire [Ascites-Q]).

• Health Resource Utilization as determined by economic analysis.

Population

The study population consists of patients greater than 18 years of age, who have cirrhosis of the liver and refractory or recurrent ascites primarily managed with periodic therapeutic paracentesis. Key contraindications include patients who have renal failure (serum creatinine >1.5 md/dL) or more than one episode of spontaneous bacterial peritonitis or bacterascites, or recurrent urinary infections over the previous 6 months.

Design and Methods

This is a multicenter, single arm within subject crossover design pivotal trial conducted in patients diagnosed with refractory or recurrent ascites who meet the inclusion/exclusion criteria. Pivotal cohort patients were evaluated for a 3-month observation period prior to implant (referred to as pre-implant observation period). All enrolled patients are followed for 24 months post alfapump implant with the primary effectiveness endpoint assessed with a comparison from Day 91 through Day 180 post pump implant (Month 4 through 6, referred to as post-implant observation period) to the pre-implant observation period. Patients with a functioning pump at 24 months are offered continued evaluation in a long-term follow-up phase which continues from 24 months through the time the pump ceases to function, pump explant, patient death, product approval or decision by the sponsor to no longer pursue approval.

A high-level summary of the timepoints defined for this study is provided for reference below:

- Day -90 to Day -1 Prior to Implant: Pre-implant Observation Period
- Day 0 (Implant) to Day 90: Stabilization Period
- Day 91 to Day 180: Post-implant Observation Period
- Month 6 to Month 24: Post 6-month Study Follow-up Period
- Year 2 onward: Optional Long-Term Follow-up

Roll-in Patients

Training in the pump implant procedure as well as other specific device training was conducted at all study centers prior to initiation of enrollment and implants in the Roll-in phase of the study. Roll-in patients were enrolled at the site until sufficient experience was obtained with the implant procedure and the site was approved by the sponsor to treat patients in the pivotal phase. Up to 3 patients were planned to be enrolled and implanted per site in this Roll-in phase to allow for the initial pump implantation and alfapump treatment experience. In the event a primary implanter at the site was replaced or added, up to 3 additional roll-in patients were allowed. Roll-in patients did not undergo the 3-month pre-implant observation period and are not included in the primary analysis set but are summarized separately for purposes of safety evaluation with effectiveness data provided as supplemental information.

Pivotal Cohort Patients

Pivotal cohort patients were evaluated in a 3-month pre-implant observation period during which they received standard of care therapy consisting of dietary sodium restriction, diuretics, and therapeutic paracentesis as required for removal of ascitic fluid. Following the initial 3-month pre-implant observation period during which the number and volume of paracenteses and patient-reported outcomes (assessed by SF-36 Physical Component Score as well as a disease-specific validated questionnaire

[Ascites-Q]) were documented, patients were reevaluated for eligibility for pump implant.

All patients (Pivotal and Roll-in) underwent a final eligibility assessment prior to pump implant. If deemed eligible, patients were implanted with the alfapump. In the immediate 3 months post-implant (post-implant stabilization period), patients were monitored with pump adjustments as needed to increase or decrease volume of fluid to be removed each day. After this period of stabilization, a 3-month primary endpoint observation period began (post-implant observation period).

Timeframe

The first patient visit occurred on 24 September 2019. On 13 September 2022, the last patient completed the 6-month follow-up visit (completion of the study primary endpoint period). Final data cut for the Primary Analysis occurred on 01 November 2023. All data that were complete through 24 months follow up as available was included in the post 6-month follow-up summary. Note that data through 12 months was complete and monitored. Data through 24 months was not yet complete and individual data is therefore subject to change.

Summary of Results

Pivotal Cohort

A total of 71 patients were enrolled in the Pivotal Cohort. Forty (40) patients were implanted with the alfapump, of which 65.0% (26/40) completed the Primary Endpoint (6-month follow-up) assessment without death or explant of the device prior to this time. The mean age of patients in the Pivotal Cohort was 63.6 ± 9.5 years, with the majority being male (65.0%, 26/40), white (95.0%, 38/40) and of non-Hispanic or Latino ethnicity (87.5%, 35/40). The mean MELD-Na score was 15.2 ± 3.8. The most common etiologies for liver cirrhosis were alcohol (47.5%, 19/40) or NASH (37.5%, 15/40). The mean duration of ascites diagnosis was 15.7 ± 14.8 months (range including up to 64.8 months), with a mean number of 3.0 ± 1.3 paracenteses in the month prior to the baseline assessment (values at screening visit). An overview of the main results by endpoint for the Pivotal Cohort is shown in the table below.

Summary of Results through 6 months - Pivotal Cohort	
Endpoint	**Main Outcome**
Primary Effectiveness (Co-Primary Endpoints)[1]	
Per-patient ratio of post-implant to pre-implant with respect to average monthly number of therapeutic paracenteses (defined as removal of ≥1.5L ascites through needle puncture of abdominal wall). *Pre-implant: Pre-implant observation period (Day -90 to Day -1) also referred to as "pre-implant period".* *Post implant: Post-implant observation period (Day 91 to Day 180) also referred to as "post-implant period".* Proportion of patients with at least 50% reduction in number of monthly therapeutic paracenteses from the pre-implant observation period to post-implant observation period.	This primary effectiveness endpoint was achieved. The median per-patient ratio (post/pre) of the average monthly number of paracentesis procedures was 0 (with a mean of 0.18, or 82% reduction on average) which was significantly lower than the targeted performance goal of 0.5 (P<0.001). The mean monthly number of paracenteses in the 3 months post-implant period was 0.2 ± 0.6 compared to 3.2 ± 1.5 mean monthly number of paracenteses in the pre-implant period. This primary effectiveness endpoint was achieved. The proportion of patients with at least 50% reduction in monthly therapeutic paracentesis in the post-implant period was significantly greater than the 50% performance goal (76.75%, 95% CI: 62.81, 90.69, P<0.001).
Primary Safety	
Combined rate of open surgical intervention/explant (requiring general anesthesia or laparotomy) due to pump system related adverse event or to restore pump functionality; pump explant (without replacement) due to pump system related adverse event; or pump system related death from time of pump implant through 6 months post-implant (as adjudicated by the Clinical Events Committee [CEC]).	The primary safety endpoint (PSE) for the Pivotal Cohort is 17.6% (95% CI: 6.76, 34.53). Six (6) PSE events were reported through 6 months, all of which were device explants (17.6%, 6/34).

Includes: open surgical pump replacement or explant requiring general anesthesia or laparotomy due to device related complications or pump failure, open surgery to address a device related complication, pump explant without replacement as a result of a device related complication. *Does not include:* catheter replacement, repositioning or revision or pump replacement or revision that does not require general anesthesia or laparotomy, open surgical re-intervention requiring general anesthesia or laparotomy for treatment of a non-pump system related adverse event, death due to liver cirrhosis that is determined not to be pump related, explant for liver transplant or because pump is no longer needed.	
Secondary Effectiveness Endpoints Intended for Potential Label Claim	
Requirement for large volume paracentesis (LVP): reduction in the average number of LVP events per month (that consist of removing ≥ 5L of ascitic fluid) in the post-implant 3-month primary endpoint observation period compared to the pre-implant observation period.	A significant reduction in the average monthly number of LVP events was observed in the 3-month post-implant period when compared to the pre-implant observation period (P<0.001). The mean monthly number of LVPs in the 3 months prior to implant was 2.3 ± 1.30 and this decreased to 0.1 ± 0.22 in the 3-month post-implant observation period (Day 91 to Day 180).
Reduction of cumulative volume of ascitic fluid removed by means of therapeutic paracentesis in the post-implant 3-month primary endpoint observation period as compared to the pre-implant 3-month observation period.	A significant reduction in the cumulative volume of ascites fluid removed by paracentesis was observed in the 3-month post-implant observation period when compared to the pre-implant observation period (P<0.001). The mean cumulative volume of ascites removed by paracentesis in the pre-implant observation period was 54.2 ± 2.3 L and this decreased to 2.8 ± 9.1 L in the post-implant observation period (Day 91 to Day 180).

Improvement in SF-36 Physical Component Score in the post-implant 3-month primary endpoint observation period as compared to the pre-implant 3-month observation period.	There was a statistically and clinically significant improvement (increase) in the SF-36 Physical Component Summary T-Score at the end of the 3-month post-implant observation period (Month 6) as compared to at the end of the pre-implant observation period ($P<0.001$), with patients on average improving by 6.4 ± 8.41 T-score points. This change is determined to meet the criteria for clinically meaningful change as defined by the SF-36 user manual as a mean change in SF-36 PCS of greater than 2 T-score points. (Maruish, M.E. (Ed.). User's manual for the SF-36v2 Health Survey (3rd ed.). Lincoln, RI: Quality Metric Incorporated.).
Improvement in Ascites-Q Score in the post-implant 3-month primary endpoint observation period as compared to the pre-implant 3-month observation period..	There was a statistically significant improvement in Ascites-Q at the end of the 3-month post-implant observation period (Month 6) as compared to at the end of the pre-implant observation period ($P<0.001$) with patients on average improving by 16.8 points reduction.. While improvement in ascites symptoms was statistically significant, it might not be clinically significant.

Additional Safety Endpoints/Assessments through 6 months	
- Safety of the alfapump implant procedure and alfapump therapy as determined by the rate of explants, re-interventions, major adverse events (MAEs) and other serious device or procedure related adverse events. - MAE is defined as acute kidney injury (AKI) > stage 2, hepatorenal syndrome, hepatic encephalopathy >grade 2, spontaneous bacterial peritonitis or recurrent or refractory infection related to the alfapump system, procedure, or therapy (as adjudicated by CEC). - Safety of the alfapump implant procedure and alfapump therapy as determined by the rate of explants, re-interventions, MAEs and other serious device or procedure related adverse events. MAE is defined as AKI > stage 2, hepatorenal syndrome, hepatic encephalopathy >grade 2, spontaneous bacterial peritonitis or recurrent or refractory infection related to the alfapump system, procedure, or therapy (as adjudicated by CEC)..	Nine (9) alfapump re-interventions (excluding explants for liver transplant) were reported in the Pivotal Cohort through the 6 months follow up (22.5%, 9/40). Of these, 7 events were explants (17.5%, 7/40), 1 was a component replacement (2.5%, 1/40) and one was a re-positioning of a device component (2.5%, 1/40). (Note that one device explant occurred due to patient non-compliance and was not considered a primary safety endpoint). After re-interventions, alfapump therapy was successfully continued. The MAE rates in the pre and post implant observation periods were similar. In the three months prior to implantation, 5 MAEs in 3 patients were reported (7.5%, 3/40) Three months post-implant (Day 91 to Day 180), 5 MAEs in 4 patients were reported (10.0%, 4/40). There were 15 device, procedure or therapy related infections in 14 patients (35.0%, 14/40) through 6 months post-implantation. Of these, 7 were considered serious (17.5%, 7/40). There were 79 serious adverse events (SAEs) in 24 patients reported (60.0%, 24/40). Thirty-nine (39) SAEs in 22 patients were considered device, procedure or alfapump therapy-related (55.0%, 22/40). The most commonly reported SAEs were reported under the system organ class of renal and urinary disorders (35.0%, 14/40) and the preferred term acute kidney injury (25%, 11/40). Another commonly reported SAE was reported under the preferred term of hepatic encephalopathy (22.5%, 9/40). There were 5 deaths reported in the Pivotal Cohort between implant and the 6-month follow-up. None of the deaths reported through 6 months were related to the alfapump device, therapy or procedure. Overall survival at 6 months was 87.2% and is comparable to survival rates reported for this patient population without the alfapump.

[1] The primary effectiveness and safety endpoints for the study include imputation for all patients who did not complete the 6 month follow up in accordance with the imputation strategy outlined in the study protocol.

Summary of Cumulative Effectiveness Data Through 24 Months – Pivotal mITT*			
Endpoint	**Data from 0 to 6 Months**	**Data from 0 to 12 Months**	**Data from 0 to 24 Months**
Freedom from therapeutic paracentesis (>1.5L)	73% of patients	65% of patients	61% of patients
Freedom from LVP	90% of patients	86% of patients	80% of patients
Number of therapeutic paracentesis procedures per month	Median of 0.0	Median of 0.0	Median of 0.0
Average volume of ascitic fluid removed with therapeutic paracentesis	Less than 1L	Less than 1L	Less than 3L
Percentage of total volume of ascitic fluid removed by the alfapump	97%	99%	87%
Evolution of renal function as assessed by eGFR	-2.5 mL/min/1.73m^2	-5.4 mL/min/1.73m^2	-6.6 mL/min/1.73m^2
Nutritional status as assessed by PSOAS Score	N/A	+3.5 cm2/m2	+ 1.4 cm2/m2
Evolution of Prealbumin values	+ 2.4 mg/dL to above critical threshold level of 10 mg/dL	+ 2.8 mg/dL to above critical threshold level of 10 mg/dL	+ 1.8 mg/dL to above critical threshold level of 10 mg/dL
Evolution of MELD-Na score	+0.8 points	+ 1.7 points	+ 2.2 points
Change in SF-36 Score PCS and MCS	+ 6.4 points in PCS +3.1 points in MCS	+ 5.1 points in PCS + 1.9 points in MCS	+ 9.3 points in PCS + 7.0 points in MCS
Change in Ascites-Q Score	-16.8 points	-14.7 points	-26.6 points

Abdominal distension satisfaction	77% of patients with 1 level or more change on the scale	83% of patients with 1 level or more change on the scale	100% of patients with 1 level or more change on the scale
Proportion of days where the patient reported satisfaction with the size of their abdomen	+ 11 additional days satisfied with abdomen	No Diary Data Collected	No Diary Data Collected
Proportion of days where the patient reports a positive global assessment of health	+ 10 Good Health Days	No Diary Data Collected	No Diary Data Collected

**This study was not designed to assess statistical or clinical significance of study endpoints other than those cited to be specifically intended for labeling claim in table above.*

Summary of Serious Adverse Events (Pivotal Cohort)

There were 110 SAEs reported in 29 patients (72.5%, 29/40) through the 12 months and 148 SAEs in 32 patients through the 24-month (80%, 32/40) follow-up. Most SAEs were reported in the first months after alfapump implantation (Figure 4-1).

Serious Adverse Events Through 24 Months – Pivotal mITT				
	12 Months Post-Implant (Days 0 to Days 365)		**24 Months Post-Implant**	
	Number of Events (N)	**Patient with Events % (n/N)**	**Number of Events (N)**	**Patient with Events % (n/N)**
Total Number of SAEs	110	72.5% (29/40)	148	80.0% (32/40)
Number of SAEs Resulting in Hospitalization or Death	110	67.5% (27/40)	136	75.0% (30/40)
Blood and lymphatic system disorders	2	5.0% (2/40)	3	5.0% (2/40)
Anaemia	2	5.0% (2/40)	2	5.0% (2/40)
Leukocytosis	0	0.0% (0/40)	1	2.5% (1/40)

Cardiac disorders	2	5.0% (2/40)	1	5.0% (2/40)
Atrial fibrillation	1	2.5% (1/40)	1	2.5% (1/40)
Cardiac arrest	1	2.5% (1/40)	1	2.5% (1/40)
Gastrointestinal disorders	14	20.0% (8/40)	20	27.5% (11/40)
Abdominal distension	1	2.5% (1/40)	1	2.5% (1/40)
Abdominal hernia	0	0.0% (0/40)	1	2.5% (1/40)
Abdominal pain	1	2.5% (1/40)	2	5.0% (2/40)
Abdominal pain upper	1	2.5% (1/40)	1	2.5% (1/40)
Abdominal wall haematoma	1	2.5% (1/40)	1	2.5% (1/40)
Gastrointestinal haemorrhage	3	7.5% (3/40)	5	7.5% (3/40)
Haemoperitoneum	1	2.5% (1/40)	1	2.5% (1/40)
Ileus	3	5.0% (3/40)	3	5.0% (2/40)
Incarcerated umbilical hernia	1	2.5% (1/40)	1	2.5% (1/40)
Pancreatitis	1	2.5% (1/40)	1	2.5% (1/40)
Rectal haemorrhage	0	0.0% (0/40)	1	2.5% (1/40)
Upper gastrointestinal haemorrhage	1	2.5% (1/40)	2	5.0% (2/40)
General disorders and administration site conditions	8	17.5% (7/40)	11	5.0% (2/40)
Implant site erosion	3	7.5% (3/40)	4	5.0% (2/40)
Implant site extravasation	1	2.5% (1/40)	1	2.5% (1/40)

Implant site pain	0	0.0% (0/40)	1	2.5% (1/40)
Incarcerated hernia	1	2.5% (1/40)	1	2.5% (1/40)
Multiple organ dysfunction syndrome	1	2.5% (1/40)	1	2.5% (1/40)
Pyrexia	1	2.5% (1/40)	2	5.0% (2/40)
Treatment noncompliance	1	2.5% (1/40)	1	2.5% (1/40)
Hepatobiliary disorders	4	10.0% (4/40)	7	17.5% (7/40)
Hepatic failure	2	5.0% (2/40)	5	12.5% (5/40)
Hepatorenal syndrome	2	5.0% (2/40)	2	5.0% (2/40)
Immune system disorders	0	0.0% (0/40)	1	2.5% (1/40)
Drug hypersensitivity	0	0.0% (0/40)	1	2.5% (1/40)
Infections and infestations	19	32.5% (13/40)	24	35.0% (14/40)
Anal abscess	1	2.5% (1/40)	1	2.5% (1/40)
Bacteraemia	1	2.5% (1/40)	2	2.5% (1/40)
Bacterascites	3	7.5% (3/40)	5	7.5% (3/40)
COVID-19	2	5.0% (2/40)	2	5.0% (2/40)
COVID-19 pneumonia	2	5.0% (2/40)	2	5.0% (2/40)
Implant site cellulitis	1	2.5% (1/40)	1	2.5% (1/40)
Peritonitis bacterial	5	12.5% (5/40)	6	12.5% (5/40)
Pneumonia	1	2.5% (1/40)	1	2.5% (1/40)

Sepsis	1	2.5% (1/40)	2	5.0% (2/40)
Urinary tract infection	2	5.0% (2/40)	2	5.0% (2/40)
Injury, poisoning and procedural complications	8	12.5% (5/40)	8	12.5% (5/40)
Device placement issue	1	2.5% (1/40)	1	2.5% (1/40)
Fall	1	2.5% (1/40)	1	2.5% (1/40)
Treatment noncompliance	1	2.5% (1/40)	1	2.5% (1/40)
Transplant rejection	1	2.5% (1/40)	1	2.5% (1/40)
Wound dehiscence	4	5.0% (2/40)	4	5.0% (2/40)
Metabolism and nutrition disorders	8	12.5% (5/40)	12	20.0% (8/40)
Acidosis	0	0.0% (0/40)	1	2.5% (1/40)
Electrolyte imbalance	2	2.5% (1/40)	2	2.5% (1/40)
Hyperglycaemia	1	2.5% (1/40)	1	2.5% (1/40)
Hyperkalaemia	4	7.5% (3/40)	5	10.0% (4/40)
Hyponatraemia	0	0.0% (0/40)	2	0.0% (0/40)
Hypovolaemia	1	2.5% (1/40)	1	2.5% (1/40)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	1	2.5% (1/40)	1	2.5% (1/40)
Hepatic neoplasm	1	2.5% (1/40)	1	2.5% (1/40)
Nervous system disorders	15	25.0% (10/40)	19	27.5% (11/40)
Hepatic encephalopathy	15	25.0% (10/40)	19	27.5% (11/40)

Product issues	1	2.5% (1/40)	1	5.0% (2/40)
Device dislocation	1	2.5% (1/40)	1	2.5% (1/40)
Device malfunction	0	0.0% (0/40)	1	2.5% (1/40)
Psychiatric disorders	1	2.5% (1/40)	1	2.5% (1/40)
Mental status change	1	2.5% (1/40)	1	2.5% (1/40)
Renal and urinary disorders	23	45.0% (18/40)	33	50.0% (20/40)
Acute kidney injury	16	35.0% (18/40)	26	40.0% (16/40)
Bladder spasm	4	10.0% (4/40)	4	10.0% (4/40)
Haematuria	2	5.0% (2/40)	2	5.0% (2/40)
Urination retention	1	2.5% (1/40)	1	2.5% (1/40)
Respiratory, thoracic and mediastinal disorders	3	7.5% (3/40)	3	7.5% (3/40)
Aspiration	23	2.5% (1/40)	1	2.5% (1/40)
Respiratory failure	23	5.0% (2/40)	2	5.0% (2/40)
Vascular disorders	1	2.5% (1/40)	1	2.5% (1/40)
Hypotension	1	2.5% (1/40)	1	2.5% (1/40)

Note: All events that occurred while the patient was active in the study are included.

Note: 1 Serious adverse events occurred after day 730 but prior to study exit among patients who did not participate in the optional long term follow-up. These events are included in the 24 month analysis.

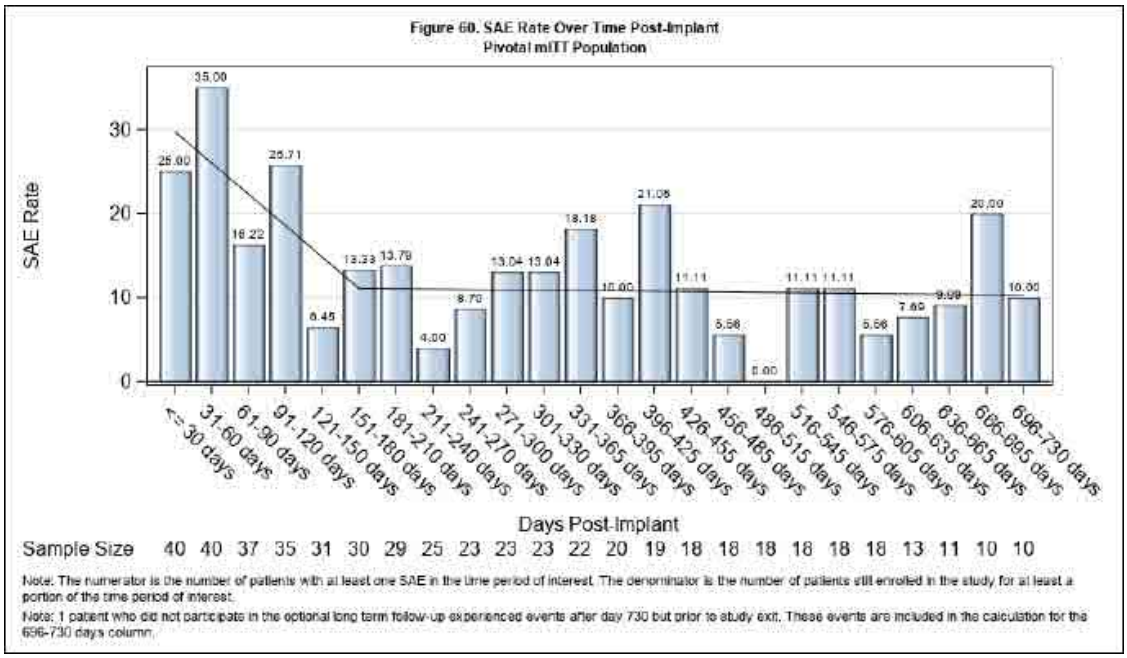


Figure 4-1: *SAE Rate over Time – Implanted Patients*

Percentage is number of subjects with at least one SAE in window divided by number of patients enrolled in study during at least one day of window.

Roll-in Cohort

A total of 39 patients were enrolled in the Roll-in Cohort. Twenty-nine (29) patients were implanted with the alfapump, of which 82.8% (24/29) completed the 6-month follow-up. The mean age of included patients in the Roll-in Cohort was 62.7 ± 8.8 years, with the majority being male (58.6%, 17/29), white (89.7%, 26/29) and of non-Hispanic or Latino ethnicity (93.1%, 27/29). The mean MELD Na score was 13.6 ± 3.6 and mean Child Pugh score was 8.0 ± 0.9. The most common etiologies for liver cirrhosis were alcohol (72.4%, 21/29) or NASH (24.1%, 7/29). The mean duration of ascites diagnosis was 21.8 ± 19.0 months, with a mean number of 3.7 ± 1.6 paracenteses in the month prior to device implantation. An overview of the main safety and effectiveness results through the 24 months is shown in the table below (Table 2). Note that no formal statistical analysis was conducted for Roll in.

Summary of Results - Roll-in Cohort	
Endpoint	**Roll-in Cohort**
Primary effectiveness and Safety Endpoints	
Primary Effectiveness Endpoint	In the month prior to implantation the average number of monthly paracenteses for the Roll-in Cohort was 3.7 ± 1.6, while in the 3 months post-implant observation period (Day 91 through Day 180), the average number of monthly paracenteses was 0.2 ± 0.3.

Primary Safety Endpoint	The PSE for the Roll-in Cohort is 15.4% (95% CI: 4.36, 34.87). Four (4) PSE events in 4 patients were reported through 6 months, 3 of which were device explants (11.5%, 3/26) and one pump system related death.
Key Secondary Effectiveness Endpoints*	
LVP Events	The average number of LVP events changed from 2.7 ± 1.38 to 0.1 ± 0.28 from the month prior to the implantation to the post-implant observation period (Day 91 to Day 180).
Ascitic volume	The cumulative volume of ascitic fluid changed from 22.8 ± 12.5 L to 2.6 ± 6.0 L between the month prior to implantation to the post-implant observation period (Day 91 to Day 180).
SF-36 Physical Component T-Score	The SF-36 Physical Component T-Score changed from 34.5 ± 6.85 to 40.2 ± 9.03 at the end of the 3-month post-implant observation period (Month 6) as compared to pre-implant.
Ascites-Q Score	The Ascites-Q Score changed from 60.0 ± 19.6 to 42.2 ± 22.3 points at 6 months compared to pre-implant.
Additional Safety Endpoints/Assessments Through 6 Months	
Re-interventions and explants	Eleven (11) alfapump re-interventions were reported in the Roll-in Cohort through the 6-month follow-up in 9 patients (31.0%, 9/29). Re-interventions included 3 component replacements (10.3%, 3/29), 3 re-positionings (10.3%, 3/29) and 5 explants (17.2%, 5/29). (Note that there were 3 explants reported for the PSE, since 2 explants were not considered a PSE: one event was a patient decision and one related to patient adherence factors.)
MAEs	There were 3 MAEs reported in 2 patients (6.9%, 2/29) through 6 months post alfapump implantation (hepatorenal syndrome was reported twice in one patient [3.4%, 1/29] and one hepatic encephalopathy > Stage 2 in one patient [3.4%, 1/29]).
Device-related infections	There were 5 device, procedure or therapy related infections in 3 patients (10.3%, 3/29) through 6 months post-implantation. Of these, 2 infections in one patient were considered serious (3.4%, 1/29).

Device-related SAEs	There were 55 SAEs reported in 20 patients (69.0%, 20/29). Of those, 28 SAEs were device, procedure or therapy related in 17 patients (58.6%, 17/29). The most commonly reported related SAE was AKI (20.7%, 6/29)..
Deaths	Two deaths were reported post-implant in the Roll-in Cohort. One patient (02-001) died due to underlying disease. Patient 12-004 developed hemorrhagic shock due to an inferior artery bleed that had delayed presentation and died at day 6 post implant. The CEC determined death was related to the implant procedure. Overall survival at 6 months in the Roll-in Cohort was 93.1%.
Safety and Effectiveness Through 24 Months	
Effectiveness	The number of monthly therapeutic paracentesis procedures was 0.2 ± 0.53 between 6- and 12-months follow-up and 0.1 ± 0.14 between 12- and 24-months follow-up The number of monthly large volume paracentesis (LVP) procedures was 0.2 ± 0.54 between 6- and 12-months follow-up and 0.0 ± 0.0 between 12- and 24-months follow-up. Mean total Ascites-Q score was 36.9 ± 21.76 points at 12 months and 33.3 ± 13.66 at 24 months from preimplant. The mean SF-36 Physical Component Summary T-Score was 37.8 ± 8.77 points at 12 months and 37.9 ± 11.22 points at 24 months.

Safety	Between 0 and 24 months, a total of 133 SAEs (93.1%, 27/29) were reported of which 48 events (72.4%, 21/29) were adjudicated to be related to the device, procedure or therapy. As with the pivotal cohort, most SAEs were reported through 6 months post alfapump implantation and the most commonly reported related SAE through the 24-month follow-up was AKI (27.6%, 8/29). Highest Stage 1: 10.3%, Stage 2: 10.3%, and Stage 3:6.9%. An additional 10 patients died, with 9 deaths related to underlying disease. One patient death was considered related to alfapump therapy (AKI with other contributory factors). An additional 6 explants were reported between 6 and 24 months. Five (5) explants were for AEs related to the alfapump device, procedure or therapy (UTI, implant sire erosion, implant site pain, and ascites). In the optional long-term follow-up one patient died due to underlying disease and 4 patients had explants (2 device no longer needed, 2 related to AEs).
* Data from the Roll-in Cohort are not used to support the secondary endpoints intended for label claim.	

Summary of Serious Adverse Events (Roll-in Cohort)

There were 54 SAEs reported through 6 months in 20 patients (69.0%, 20/29, Table 36) The most commonly reported SAEs were reported under the SOC renal and urinary disorders (41.4%, 12/29) and AKI (27.6%, 8/29).

Serious Adverse Events through 6 Months – Roll-in		
	Number of Events N	**Patients with Events % (n/N)**
Total Number of SAEs	54	69.0% (20/29)
Number of SAEs Resulting in Hospitalization or Death	49	62.1% (18/29)
Blood and lymphatic system disorders	1	3.4% (1/29)
Anaemia	1	3.4% (1/29)
Cardiac disorders	1	3.4% (1/29)

Angina pectoris	1	3.4% (1/29)
Gastrointestinal disorders	7	17.2% (5/29)
Abdominal hernia obstructive	1	3.4% (1/29)
Ascites	3	6.9% (2/29)
Ileus	1	3.4% (1/29)
Ileus paralytic	1	3.4% (1/29)
Umbilical hernia perforation	1	3.4% (1/29)
General disorders and administration site conditions	7	17.2% (5/29)
Asthenia	1	3.4% (1/29)
Implant site erosion	1	3.4% (1/29)
Implant site pain	1	3.4% (1/29)
Incarcerated hernia	2	3.4% (1/29)
Oedema peripheral	1	3.4% (1/29)
Systemic inflammatory response syndrome	1	3.4% (1/29)
Hepatobiliary disorders	2	3.4% (1/29)
Hepatorenal syndrome	2	3.4% (1/29)
Infections and infestations	5	3.4% (1/29)
Abdominal hernia infection	1	3.4% (1/29)
Bacterascites	1	3.4% (1/29)
Implant site cellulitis	1	3.4% (1/29)
Urinary tract infection	1	3.4% (1/29)
Incarcerated hernia	1	3.4% (1/29)
Injury, poisoning and procedural complications	7	17.2% (5/29)
Arterial injury	1	3.4% (1/29)
Device placement issue	2	3.4% (1/29)
Post procedural haemorrhage	1	3.4% (1/29)
Subdural haematoma	1	3.4% (1/29)
Wound dehiscence	1	3.4% (1/29)
Metabolism and nutrition disorders	6	10.3% (3/29)
Electrolyte imbalance	1	3.4% (1/29)
Hyponatraemia	5	6.9% (2/29)
Nervous system disorders	2	3.4% (1/29)
Hepatic encephalopathy	2	3.4% (1/29)
Renal and urinary disorders	14	41.4% (12/29)
Acute kidney injury	8	27.6% (8/29)
Bladder spasm	1	3.4% (1/29)
Haematuria	3	10.3% (3/29)
Urinary retention	2	6.9% (2/29)

Respiratory, thoracic and mediastinal disorders	1	3.4% (1/29)
Respiratory failure	1	3.4% (1/29)
Bladder spasm	1	3.4% (1/29)
Vascular disorders	1	3.4% (1/29)
Hypotension	1	3.4% (1/29)
Note: All events that occurred while the patient was active in the study are included.		

Conclusion

Overall, implantation with the alfapump in patients with refractory or recurrent ascites meaningfully reduced the need for therapeutic paracentesis and also improved ascites symptoms (while statistically significant this might not be clinically meaningful) and subjective physical health (both statistically significant and clinically meaningful) at 6 month follow up as compared to pre-implant. Results from the Primary Endpoint analysis showed that the vast majority of patients no longer needed therapeutic paracentesis after the alfapump implant. Primary safety events were within the anticipated range for this high-risk patient population and the mortality rate and rate of serious adverse events is similar to that observed in patients managed using standard of care with paracentesis for recurrent and refractory ascites. Risks, mainly acute kidney injury and infection, are mitigated through careful monitoring and patient management while the alfapump is in place. The results to date beyond the Primary Endpoint analysis (>6 months), remained consistent with those reported for the first 6 months and do not raise additional concerns associated with safety of the alfapump System. Overall, based on the information available at the time of writing this report (data cutoff), the results support a benefit of the alfapump by providing a reduction in therapeutic paracentesis and by improving ascites symptoms[2] and subjective physical health.

[2] While improvement in ascites symptoms was statistically significant, it might not be clinically significant.

5. Support and Service

5.1 Contact Information

Swiss Technical Office:

Sequana Medical NV

Technoparkstrasse 1

8005 Zurich Switzerland

Phone: +41 44 403 55 00

For general inquiries or to request additional training, we can also be reached via email at info@sequanamedical.com.

Customer Service:

Sequana Medical US Inc.

265 Franklin Street , Suite 1702

Boston, MA 02110

USA

Phone: +1 617-963-5280

In the event of device and cybersecurity concerns, reach us via email at

vigilance@sequanamedical.com.

5.2 Maintenance and Safety Checks

Caution: *The device and implantable components may not be re-sterilized and should be returned to Sequana Medical if proper function is in question.*

Caution: *Make sure to examine* ***alfa****pump® and catheter packages upon delivery and also prior to implantation.*

All components of the **alfa**pump® System must be handled with care. Sterile products must not be opened before use and cannot be cleaned, as cleaning sterile products may compromise sterility. Sterile products may not be re-sterilized.

If parts of the **alfa**pump® System are dropped or stored in temperatures outside of the allowed range, their functioning can be impaired. Please refer to section **"1.8 Warnings and Precautions"** for information on proper storage and handling.

All non-sterile products like the **alfa**pump® Programmer IV, its Power supply, the USB cable, Power cords, the Smart Charger and the Docking Station may all be cleaned with a damp cloth. Mild soap or cleaner is also acceptable, but do not use any strong solvent. All non-sterile products may be cleaned in this way as often as you like.

If any problems arise with the **alfa**pump® System components or accessories, please contact Sequana Medical's customer service or your local field clinical representative.

Please describe the problem in writing and keep useful records ready, making note of any error messages.

Changes or modifications not expressly approved by the party responsible for compliance could void the user's authority to operate the equipment.

No special maintenance action is required to maintain the basic safety of the Smart Charger and its accessories, including the **alfa**pump® Programmer IV, with regard to electromagnetic disturbances throughout its expected service life (24 months).

5.3 alfapump® System Components

The **alfa**pump® System is intended to be used with the following components available from Sequana Medical.

Accessories	Comment	Part no.
alfapump®	Implantable pump	01473
alfapump® System Instructions for Use	Laguages: EN, ES	01464
Smart Charger	Hand-held paddle	01475
Docking Station	Stand and charger for Smart Charger	01476
Smart Charger Instructions for Use	Laguages: EN, ES	01463
alfapump® Programmer IV	Tablet to run FlowControl Software	02403
Medical Grade Power supply	90-264 VAC	02398
Proprietary USB cable	2.00 m	01482
Smart Charger USB-C Cable	2.00 m	02399
alfapump® Programmer IV Instructions for Use	Laguages: EN, ES	02462
Power Cord Type A	2.00 m	00963
Catheter Extension Connector	Titanium	01479
Peritoneal Catheter Extension	Blue	01481
Bladder Catheter Extension	Yellow	01480
Catheter Locking Cap	PEEK	01483
Tunneling Rod	Stainless steel	01478
Bladder Catheter	Yellow	01474
Peritoneal Catheter SNCA-5262L	Transparent	01991
Introducer Kit	Two pieces are provided	02155

5.4 Note on Waste Disposal

The **alfa**pump® contains a rechargeable lithium-ion battery which has an operating life of over 3 years. The battery is not accessible for medical personnel, so please return all explanted **alfa**pumps and catheters to Sequana Medical for testing and disposal. Please also return **alfa**pump® Programmer IV devices, which are no longer needed, to Sequana Medical.

Other accessories should be disposed of in accordance with your clinic's standard regulations.

Please contact Sequana Medical's customer service or your local field clinical representative if there are any questions.

5.5 alfapump® System Technical Specifications

alfapump®:

Size:	75 mm (L) x 50 mm (W) x 18 mm (H)
Volume:	55 cm^3
Weight:	< 100 g
Battery:	Lithium Ion single cell, rechargeable: 4.1 V / 200 mAh
Materials (in contact):	PEEK, stainless steel 1.4441, polyester, UPC15
Charge time:	< 5 h when battery is completely depleted / 30 minutes daily in standard use

Radio Transmission:

Frequency	Transmission Power	Transfer Rate	Modulation	Duty Cycle
915 MHz (USA/CA)	-7 dBm	76.8 kbit/s	GFSK	100 %

Environmental conditions for storage (**alfa**pump®):

Temperature:	41°F to 80°F
Humidity:	20% to 80%
Pressure:	70 kP ± 3,5 kP to 150 kP ± 3,5 kP

Note: *Keep away from sunlight.*

Bladder Catheter and Peritoneal Catheter SNCA-5262L:

For use only with the **alfa**pump® System.

Bladder Catheter materials:	Implant grade silicone, yellow, polyester
Peritoneal Catheter SNCA-5262L materials:	Implant grade silicone, transparent, polyester
Outer diameter:	4.84 mm / 4.95 mm
Inner diameter:	2.6 mm
Internal volume:	0.05 ml/cm
Maximal pull force:	10 N

Environmental conditions for storage:

Temperature:	41°F to 80°F
Humidity:	20% to 80%
Pressure:	70 kP ± 3,5 kP to 150 kP ± 3,5 kP

Note: *Keep away from sunlight.*

Tunneling Rod:

Materials:	Stainless steel
Outer diameter:	5 mm
Length:	250 mm

Environmental conditions for storage:

Temperature:	41°F to 80°F
Humidity:	20% to 80%
Pressure:	70 kP ± 3,5 kP to 150 kP ± 3,5 kP

Note: *Keep away from sunlight.*

Implant Accessories:

Bladder Catheter Extension:

Materials:	Implant grade silicone (yellow and blue)
Length:	40 cm

Peritoneal Catheter Extension:

Materials:	Implant grade silicone (yellow and blue)
Length:	30 cm

Catheter Extension Connector:

Materials:	Titanium

Environmental conditions for transport and storage:

Temperature:	41°F to 80°F
Humidity:	20% to 80%
Pressure:	70 kP ± 3,5 kP to 150 kP ± 3,5 kP

Note: *Keep away from sunlight*

Introducer Kit:

Introducer Needle:

Material:	Stainless steel
Outer Diameter:	1.3 mm
Inner Diameter:	1.1 mm
Effective Length:	70 mm

Guidewire:

Material:	Stainless steel
Outer Diameter	0.96 mm
Nominal Length	47.5 cm

18 F Dilator:

Material	High density polyethylene with ca. 15 % $BaSO_4$
Outer Diameter	6.1 mm
Inner Diameter	1.0 mm

14 F Dilator:

Material	High density polyethylene with ca. 15 % BaSO4
Outer Diameter	4.7 mm
Inner Diameter	1.0 mm

10 F Dilator:

Material	High density polyethylene with ca. 15 % BaSO4
Outer Diameter	3.3 mm
Inner Diameter	1.0 mm

Environmental conditions for transport and storage:

Temperature:	41°F to 80°F
Operating humidity:	20% to 80%
Atmospheric pressure:	70 kP ± 3,5 kP to 150 kP ± 3,5 kP

Note: *Keep away from sunlight.*

5.6 Maintenance and Service

No further maintenance or service is required; there are no parts which can be individually serviced or repaired. If a device appears to be damaged or no longer sterile, please return it to Sequana Medical.

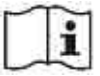
EN

6. Appendices

6.1 Appendix A - Explanations of Symbols used in the alfapump® System

Refer to the labels to see which symbols apply to which part of the **alfa**pump® System.

Symbol	Standard Reference	Symbol Title	Explanatory Text
	ISO 15223-1, Clause 5.1.1 ISO 7000 (Symbol No. 3082)	Manufacturer	Identifies the medical device manufacturer.
	ISO 15223-1, Clause 5.1.3 ISO 7000 (Symbol No. 2497)	Date of Manufacture	Indicates the date on which the medical device was manufactured.
	ISO 15223-1, Clause 5.7.7	Medical device	Indicates that the item is a medical device.
	ISO 15223-1, Clause 5.1.4 ISO 7000 (Symbol No. 2607)	Use By Date	Indicates the date after which the medical device is not to be used.
	ISO 15223-1, Clause 5.1.6 ISO 7000 (Symbol No. 2493)	Catalogue or Model Number	Indicates the manufacturer's catalogue number so the medical device can be identified.
	ISO 15223-1, Clause 5.1.7 ISO 7000 (Symbol No. 2498)	Serial Number	Indicates the manufacturer's serial number so a specific medical device can be identified.
	ISO 15223-1, Clause 5.1.5 ISO 7000 (Symbol No. 2492)	Batch Code	Indicates the manufacturer's batch or lot code.
	ISO 15223-1, Clause 5.2.3 ISO 7000 (Symbol No. 2501)	Sterilized using Ethylene Oxide	Indicates the medical device has been sterilized using ethylene oxide.
	ISO 15223-1 Clause 5.2.13 ISO 7000 (Symbol No. 3708)	Single sterile barrier system with protective packaging inside	Indicates there is a single sterile barrier system with protective packaging inside.
	ISO 15223-1 Claus 5.3.2 ISO 7000 (Symbol No. 0624)	Keep away from sunlight	Indicates the medical device needs protection from light sources.
	ISO 15223-1, Clause 5.3.7 ISO 7000 (Symbol No. 0632)	Temperature Limit	Indicates the temperature limits to which the medical device can be safely exposed.

	ISO 15223-1, Clause 5.3.8 ISO 7000 (Symbol No. 2620)	Humidity Limitation	Indicates the range of humidity to which the medical device can be safely exposed.
	ISO 15223-1, Clause 5.3.9 ISO 7000 (Symbol No. 2621)	Atmospheric pressure limitation	Indicates the range of atmospheric pressure to which the medical device can be safely exposed.
	ISO 15223-1, Clause 5.3.4 ISO 7000 (Symbol No. 0626)	Keep dry	Indicates the medical device needs to be protected from moisture.
	ISO 15223-1, Clause 5.3.1 ISO 7000 (Symbol No. 0621)	Fragile, Handle with Care	Indicates the medical device can be broken or damaged if not handled with care.
	ISO 15223-1, Clause 5.4.2 ISO 7000 (Symbol No. 1051)	Do not re-use	Indicates the medical device is intended for one use, or for use on a single patient during a single procedure.
	ISO 15223-1, Clause 5.2.6 ISO 7000 (Symbol No. 2608)	Do not resterilize	Indicates the medical device should not be resterilized.
	ISO 15223-1, Clause 5.7.3	Patient identification	Indicates the identification data of the patient.
	ISO 15223-1, Clause 5.7.4 ISO 7000 (Symbol No. 3705)	Patient information website	Indicates a website where a patient can obtain additional information on the medical product.
	ISO 15223-1, Clause 5.7.5	Health care centre or doctor	Indicates the address of the health care centre or doctor where medical information about patient may be found.
	ISO 15223-1, Clause 5.7.6	Date	Indicates the date that information was entered or a medical procedure took place.
	ISO 15223-1, Clause 5.2.8 ISO 7000 (Symbol No. 2606)	Do not use if package is damaged and consult instructions for use	Indicates the medical device should not be used if the package is damaged or opened and the user should consult the instructions for use.
	ISO 15223-1, Clause 5.4.3 ISO 7000 (Symbol No. 1641)	Consult Instructions for Use	Indicates the need for the user to consult the instructions for use.

	IEC 60601-1 ISO 7010 (Symbol No. M002)	Refer to instruction manual/ booklet	Indicates the user must consult the instructions for use.
	ISO 15223-1 Clause 5.7.10	Unique device identifier	Indicates a carrier that contains unique identifier information.
	ASTM F2503	Magnetic Resonance (MR) Unsafe	Indicates the medical device is MR Unsafe and should be kept away from magnetic resonance (MR) imaging equipment.
	IEC 60601-1, Table D.1 (Symbol No. 20) IEC 60417 (Symbol No. 5333)	Type BF Applied Part	Identifies a type BF applied part complying with IEC 60601-1.
	IEC 60601-1, Table D.1 (Symbol No. 1) IEC 60417 (Symbol No. 5032)	Alternating current	Indicates that the equipment is suitable for alternating current only; to identify relevant terminals.
	IEC 60601-1, Table D.1 (Symbol No. 4) IEC 60417 (Symbol No. 5031)	Direct current	Indicates that the equipment is suitable for direct current only; to identify relevant terminals.
	IEC 60601-1, Table D.3 (Symbol No. 2) IEC 60529	Degree of protection	Manufacturer-determined degree of particle and water ingress protection, where: N1= degree of protection from particulates (scale of 0-6); and N2 = degree of protection from water (scale of 0-8) NOTE When a characteristic numeral is not required to be specified, it is replaced by the letter "X".
	IEC 60601-1, Table D.1 (Symbol No. 9) IEC 60417 (Symbol No. 5172)	Class II equipment	Identifies equipment meeting the safety requirements specified for Class II equipment according to IEC 61140.
	IEC 60417 (Symbol No. 5134) ISO 7000 (Symbol No. 5134)	Electrostatic sensitive devices	Indicates electrostatic sensitive devices on packages containing them or on the device itself.

	IEC 60417 (Symbol No. 5140) ISO 7000 (Symbol No. 5140)	Non-ionizing electromagnetic radiation.	Indicates generally elevated, potentially hazardous, levels of non-ionizing radiation, or to indicate equipment or systems e.g. in the medical electrical area that include RF transmitters or that intentionally apply RF electromagnetic energy for diagnosis or treatment.
	IEC 60417 (Symbol No. 5957)	For indoor use only	Identifies electrical equipment designed primarily for indoor use.
	21 CFR 801.15(c)(1)(i)F 21 CFR 801.109	Prescription Use Only	Caution: Federal law (USA) restricts this device to sale by or on the order of physician. (CFR 21 801.109)
	IEC 60601-1, Annex D (Symbol No. 14)	"ON"/"OFF" button	Smart Charger's "ON"/"OFF" button
	/	Sequana Medical's symbol for the **alfa**pump® System	Indicates that the device is part of the **alfa**pump® System

6.2 Appendix B - Manufacturer's Declaration for the alfapump® System

Electromagnetic compatibility (EMC)

The **alfa**pump® System comprises the Smart Charger and its accessories, including the **alfa**pump® Programmer IV. Therefore, please take into consideration the following information related to electromagnetic compatibility.

WARNING: The **alfa**pump® System needs to be installed and put into service according to the EMC information provided in the next tables. Precautions to be taken to prevent adverse events due to electromagnetic disturbances include ensuring that power input voltage and line frequency are within the defined range according to the intended use of the device. For precautions related to the EMC environment, please refer to the "Electromagnetic Environment Guidance" column of the tables below.

WARNING: Portable and mobile RF communications equipment can affect the **alfa**pump® System (including peripherals such as antenna cables and external antennas) should be used no closer than 30 cm (12 inches) to any part of the can affect the **alfa**pump® System. Otherwise, degradation of performance may result.

WARNING: The use of cables, power supplies, accessories other than those specified by the manufacturer may result in increased electromagnetic emissions and/or decreased electromagnetic immunity and it may result in improper operation.

WARNING: The **alfa**pump® System should not be used adjacent to or stacked with other equipment and that if adjacent or stacked use is necessary, the **alfa**pump® System should be observed to verify normal operation in the configuration in which it will be used.

WARNING: The use of cables, power supplies, accessories other than those specified by the manufacturer may result in increased emission and/or decreased immunity.

No Essential Performance has been defined for the **alfa**pump® System. Therefore, no loss of or degradation of Essential Performance of the **alfa**pump® System are to be expected due to electromagnetic disturbances.

Please refer to Chapter 4.3 for the **alfa**pump® System's components. For further information regarding electromagnetic compatibility, please consult the *Instructions for Use of the Smart Charger* and the *Instructions for Use of the **alfa**pump® Programmer IV*.

Guidance and Manufacturer's Declaration / electromagnetic Emission - Table 201 Medical Device according to group 1/class B, tested according to CISPR 11

The **alfa**pump® System is suitable for use in the specified electromagnetic environment. The customer and/or user of the **alfa**pump® System should ensure that it is used in an electromagnetic environment as described below.

Emission test (IEC 60601-1-2 4.1 edition)	Compliance	Electromagnetic Environment Guidance
RF emission CISPR 11	Group 1	The **alfa**pump® System uses RF energy only for internal function. Therefore, RF emissions are very low and are not likely to cause any interference in nearby electronic equipment.
RF emission CISPR 11	Class A	The **alfa**pump® System is suitable for use in a hospital environment.
Harmonic emissions EN 61000-3-2	Class A	
Flicker emissions EN 61000-3-3	Complies	

The **alfa**pump® System, including the **alfa**pump® Programmer IV, is intended to be used in a hospital environment.

The emissions characteristics of this equipment make it suitable for use in industrial areas and hospitals (CISPR 11 class A). If it is used in a residential environment (for which CISPR 11 class B is normally required) this equipment might not offer adequate protection to radio-frequency communication services. The user might need to take mitigation measures, such as relocating or re-orienting the equipment.

Guidance and Manufacturer's Declaration / electromagnetic Immunity - Table 202 See sub-clauses 6.8.201 a) 3.)

The **alfa**pump® System is suitable for use in the specified electromagnetic environment. The customer and/or user of the **alfa**pump® System should ensure that it is used in an electromagnetic environment as described below.

Immunity Test Standard (IEC 60601-1-2 4.1 edition)	IEC 60601-1-2 Test-Level	Compliance-Level	Electromagnetic Environment Guidance
Electrostatic discharge (ESD) *EN 61000-4-2*	± 8 kV contact ± 2 kV, ± 4 kV, ± 8 kV ± 15 kV air	± 8 kV contact ± 15 kV air	Floors should be wood, concrete or ceramic tile. If floors are covered with synthetic materials, the relative humidity should be at least 30 %.

Electrical fast transient *EN 61000-4-4*	± 2 kV for power supply lines ± 1 kV for USB lines	± 2 kV for power supply lines ± 1 kV for USB lines	Mains power quality should be that of a typical commercial or hospital environment. If the user of the **alfa**pump® System requires correct display functions, it is recommended to filter the power supply line.
Surge *EN 61000-4-5*	L-N: ± 1 kV	L-N: ± 1 kV	
Power frequency magnetic field (50 Hz/60 Hz) *EN 61000-4-8*	30 A/m	30 A/m	Power frequency magnetic fields should be at levels characteristic of a typical location in a typical commercial or hospital environment.
Voltage dips, short interruptions on power supply input lines *EN 61000-4-11*	**Voltage dips** 0° U_T (0.5 cycles) at 0°, 45°, 90°, 135°, 180°, 225°, 270°, 315° 0° U_T (1 cycle) and 70% U_T (25/30 cycles) at 0° **Voltage interruptions** 0° U_T (250/300 cycles)	**Voltage dips** 0° U_T (0.5 cycles) at 0°, 45°, 90°, 135°, 180°, 225°, 270°, 315° 0° U_T (1 cycle) and 70% U_T (25/30 cycles) at 0° **Voltage interruptions** 0° U_T (250/300 cycles)	Main power quality should be that of a typical commercial or hospital environment if the user of the **alfa**pump® System requires continued operation during power mains interruption, it is recommended to power the device from a battery or USV.
Radiated fields in close proximity *EN 61000-4-39*	8 A/m at 30 kHz 65 A/m at 134.2 kHz 7.5 A/m at 13.56 kHz	8 A/m at 30 kHz 65 A/m at 134.2 kHz 7.5 A/m at 13.56 kHz	

Note: *U_T is the a.c. mains voltage prior to application of the test level*

Guidance and Manufacturer's Declaration / electromagnetic Immunity

The **alfa**pump® System is intended for use in the electromagnetic environment specified below. The customer and/or user of the **alfa**pump® System should assure that it is used in such an environment.

Portable and mobile RF communications equipment should be used no closer to any part of the alfapump® System, including cables, than the recommended separation distance calculated from the equation applicable to the frequency of the transmitter.			
Immunity Test Standard (IEC 60601-1-2 4.1 edition)	**IEC 60601-1-2** **Test-Level**	**Compliance-Level**	**Recommended Separation Distance**
Conducted RF IEC 61000-4-6	3 V 150 kHz to 80 MHz 6 V (ISM bands between 150 kHz and 80 MHz)	3 V 150 kHz to 80 MHz 6 V (ISM bands between 150 kHz and 80 MHz)	d = 0.35 √P 150 kHz to 80 MHz
Radiated RF IEC 61000-4-3 *Additional test frequencies according to Table 9 of IEC 60601-1-2*	3 V/m (hospital environment) 80 MHz to 800 MHz	3 V/m (hospital environment) 80 MHz to 800 MHz	d = 0.35 √P 80 MHz to 800 MHz
	3 V/m (hospital environment) 800 MHz to 2,7 GHz	3 V/m (hospital environment) 800 MHz to 2,7 GHz	d = 0.7 √P 800 MHz to 2,7 GHz
Where P is the maximum output power rating of the transmitter in watts (W) according to the transmitter manufacturer and d is the recommended separation distance in meters (m). Field strengths from fixed RF transmitters, as determined by an electromagnetic site survey, a should be less than the compliance level in each frequency range. b Interference may occur in the vicinity of equipment marked with the following symbol: 			
Note: These guidelines may not apply in all situations. Electromagnetic propagation is affected by absorption and reflection from structures, objects and people.			

[a] Field strengths from fixed transmitters, such as base stations for radio (cellular/cordless) telephones and land mobile radios, amateur radio, AM and FM radio broadcast and TV broadcast cannot be predicted theoretically with accuracy. To assess the electromagnetic environment due to fixed RF transmitters, an electromagnetic site survey should be considered. If the measured field strength in the location in which the Smart Charger with the **alfa**pump® System is used exceeds the applicable RF compliance level above, the **alfa**pump® System should be observed to verify normal operation. If abnormal performance is observed, additional measures may be necessary, such as re-orienting or relocating the **alfa**pump® System.

Wireless functions and wireless technology

The Smart Charger P5 and **alfa**pump can wirelessly communicate. Communication takes place through the Smart Charger P5, which serve as the primary interface for communication and charging of the **alfa**pump. The Smart Charger P5 transmits power transcutaneously to and communicates via RF with the **alfa**pump. Each time the patient charges the alfapump, its pump performance data is automatically transferred to the Smart Charger P5.

The wireless radio communication between the Smart Charger P5 and the **alfa**pump is based on a single channel communication at a frequency of 907±1 MHz with a maximum transmission power of 5mW. This is a usable frequency within the 915 MHz radio band according to local regulations in US and Canada. The SRD RF link incorporated in the **alfa**pump System is technically implemented via one RF chip in the implant and another in the Smart Charger P5.

Summary of wireless functionalities

RF communication between alfapump and Smart Charger P5 allows:

1. Download performance data from the implantable device to the Smart Charger P5;
2. Set new treatment parameters (including target session volume, maximum daily volume, time segments for alfapump to be active, power on/off the treatment).

The Smart Charger P5 transmits power transcutaneously to the **alfa**pump to recharge the pump internal rechargeable battery across the patient's skin at 296 kHz.

Radio communication specifications and operating characteristics

Smart Charger P5:

Description	Frequency / Frequency band (MHz)	RX bandwidth	Modulation	Effective radiated power
Radio communication	915	230 kHz	GFSK	0.224 mW
UMTS/LTE module	700/850/900/ 1700/1900/2100	/	GMSK / 8-PSK	1.6 W 0.9 W

alfapump®:

Description	Frequency / Frequency band (MHz)	RX bandwidth	Modulation	Effective radiated power
Radio communication	915	230 kHz	GFSK	0.019 mW

Quality of Service

The wireless coexistence of the **alfa**pump System was tested with acceptable results according to ANSI C63.27. These key performance indicators were monitored during the wireless coexistence tests and define the Quality-of-Service of the **alfa**pump System for a safe and effective operation:

Name	Description
RSSI	Received signal strength indicator
PER	Packet Error Rate: number of incorrectly received data packets
Time to complete requests	Elapsed time that occurs from sending a request and receive the response for the same request

Wireless coexistence acceptance criteria are reported in table below:

Required Bit rate	RSSI	PER	Time to complete requests
> 4.6 kbit/s	Min -80dBm	Max 50% of total packets	Max 10 minutes

Security of the **alfa**pump System is addressed through:

- Unique ID and pairing mechanism
- Cyclic redundancy check for data integrity
- Absence of patient demographic and hospital info from any transferred data
- Hardware and software design implementation with redundancies for data storage and transfer.

Recommended separation distances between portable and mobile RF communications equipment and the alfapump® System for equipment that is not life supporting.

The **alfa**pump® System is intended for use in the electromagnetic environment in which radiated RF disturbances are controlled. The customer or the user of the **alfa**pump® System can help prevent electromagnetic interference by maintaining a minimum distance between portable and mobile RF communications equipment (transmitters) and the **alfa**pump® System as recommended below, according to the maximum output power of the communication equipment.

Output power rating of the transmitter (PTrans.) [W]	Separation distance (depending on transmitter frequency) [m]		
	50 kHz to 80 MHz d=0.35*√P Trans [m]	80 MHz to 800 MHz d=0.35* √P Trans [m]	800 MHz to 2.5 GHz d=0.37* √P Trans [m]
0.01	0.035	0.035	0.0703
0.1	0.11	0.11	0.22
1	0.35	0.35	0.70
2	0.49	0.49	0.99
10	1.1	1.1	2.2
100	3.5	3.5	7.0
For transmitters rated at a maximum output power not listed above, the recommended separation distance d in meters (m) can be estimated using the equation applicable to the frequency of the transmitter, where P is the maximum output power rating of the transmitter in watts (W) according to the transmitter manufacturer. Note 1: At 80MHz and 800MHz, the separation distance for the higher frequency range applies. Note 2: These guidelines may not apply in all situations. Electromagnetic propagation is affected by absorption and reflection from structures, objects and people.			

Field strength from fixed RF transmitters, as determined by an electromagnetic site survey, should be less than the compliance level in each frequency range.

Interference may occur in the vicinity of equipment marked with the following symbol:

WARNING: **alfa**pump® System may be interfered with other equipment, even if that other equipment complies with CISPR emission requirements.

WARNING: RF sources in the vicinity of the device (for example, electromagnetic security systems, cellular telephones, RFID or other in-band transmitters) might interfere with the alfapump System, causing operational complications.

WARNING: Portable RF communications equipment (including peripherals such as antenna cables and external antennas) should be used no closer than 30 cm (12 inches) to any part of the Smart Charger, including cables specified by the manufacturer. Otherwise, degradation of the performance of this equipment could result.

WARNING: In case of wireless issue, it is recommended to move away from other potential portable and mobile RF communications equipment. Restart the Smart Charger and check device symbols and indicators. In case problem persists, please contact Sequana Medical Customer Service (see Customer Service contacts, Chapter 5.1).

Manufacturer's Declaration of Conformity - 47 CFR § 2.1077 Compliance Information

Unique Identifier: alfapump, Part No.: 01473

FCC ID: 2BDJN01473

Responsible Party – U.S. Contact Information:

Americas Compliance consulting, LLC dba iCertifi

FCC FRN: 0033399411

2445 NE Division Street, Suite 202

Bend, Oregon (OR)

97703, United States

Tel: 866-885-4575

Email: fccagent@icertifi.com

FCC Compliance Statement:

This device complies with Part 15 of the FCC Rules. Operation is subject to the following two conditions: (1) This device may not cause harmful interference, and (2) this device must accept any interference received, including interference that may cause undesired operation.

6.3 Appendix C - Imprint

Legal Manufacturer:

Sequana Medical NV

Kortrijksesteenweg 1112

9051 Sint-Denijs-Westrem

Belgium

Phone: +32 9 298 2828

For general inquiries, we can also be reached via email at

info@sequanamedical.com.

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

Sequana Medical's alfapump® system, and methods of use thereof, is covered by one or more of the patents referenced at www.sequanamedical.com/patents. This webpage serves as notice under 35 U.S.C. § 287(a) of patent marking.

Other patents pending.

QCBD 01464_CR21013 Rev 01.70