FLOWONIX PLAYBOOK

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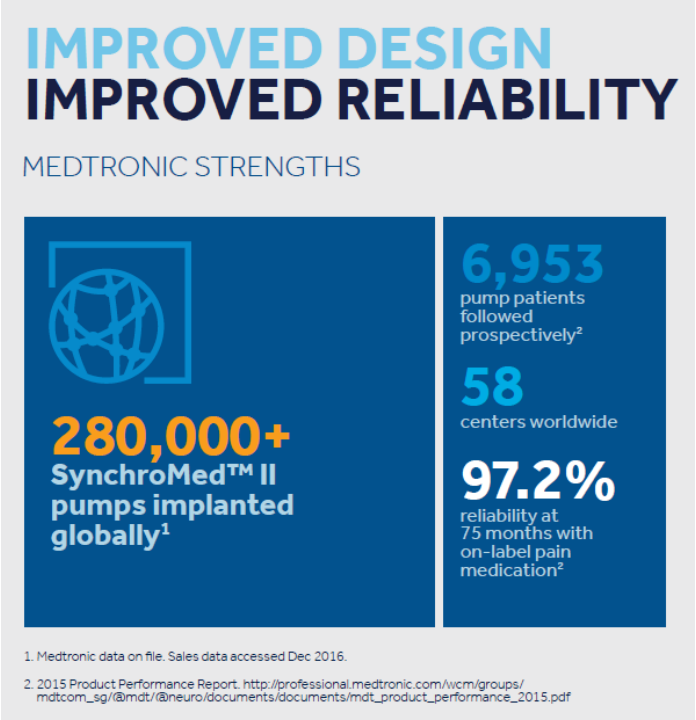
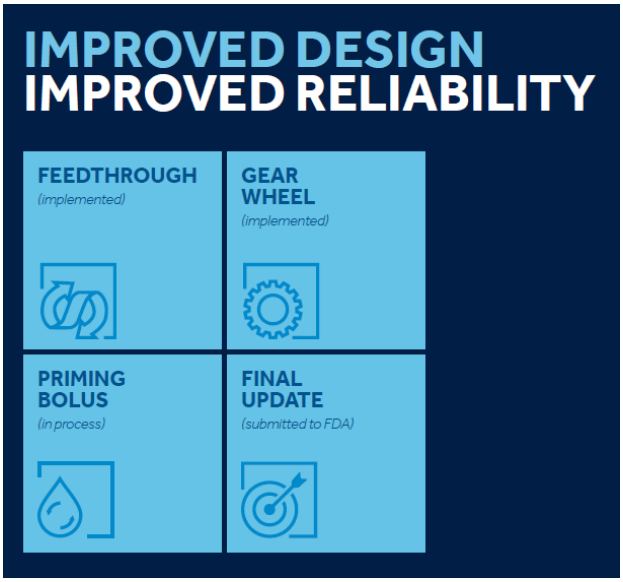
Medtronic
Further, Together

UC201711593bEN

TARGETED DRUG DELIVERY MESSAGING
RELIABILITY





- Flowonix can tell a story, but they can't compete when you compare the facts. ***Medtronic actively tracks the performance of SynchroMed™ II***, while others use ***reactive device management*** and respond only when issues occur. Be confident in your messaging.

- Use the following responses to clearly define Accuracy and respond to Flowonix claims.

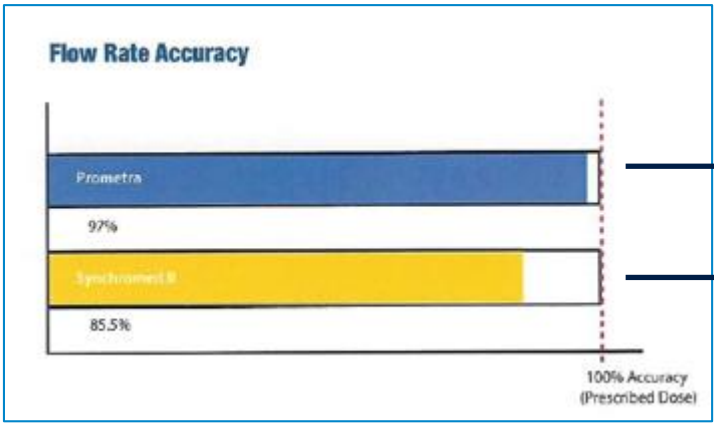
- Take your next opportunity to turn the conversation around. Do not let Flowonix capitalize on our bad press by misrepresenting the facts.

Resource: ***SynchroMed™ II Durable Design Update iPDF***

#1 ACCURACY
FLOWONIX CLAIM AND MEDTRONIC RESPONSE

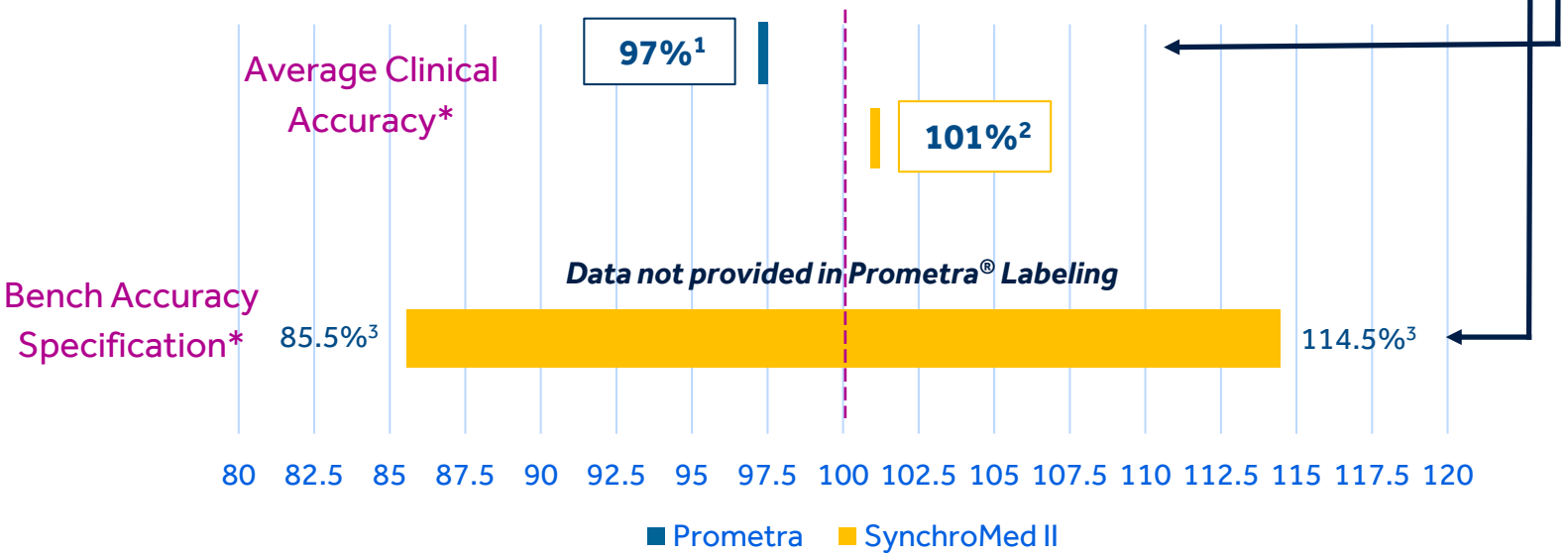
Flowonix Claim:

- Flow rate accuracy is 97% for the Prometra® pump and 85.5% for the SynchroMed™ II pump (see chart).



Medtronic Response:

- There are 2 ways to measure accuracy - **Clinical Accuracy** (clinical results) and **Bench Accuracy** (design specifications).
- In the chart above, Flowonix is comparing their average Clinical Accuracy to the lower parameter of our Bench Accuracy. It is apples to oranges and misleading.



*Based upon studies conducted for each product and as further reflected in each product's labeling. No clinical head-to-head studies have been performed comparing SynchroMed™ and Prometra®.

Resource: ***Quality Demonstrated Sell Sheet***

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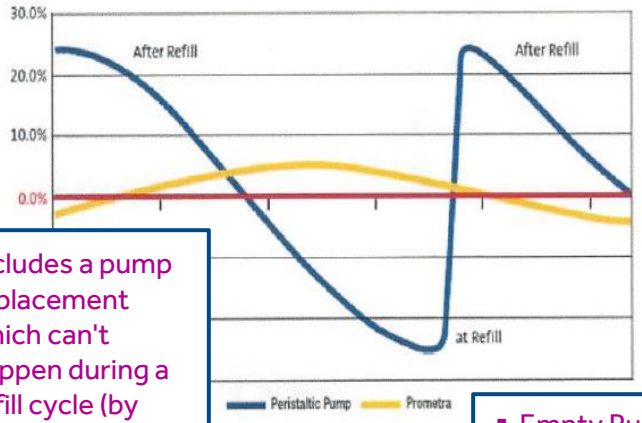
#2 ACCURACY/PRECISION
FLOWONIX CLAIM AND MEDTRONIC RESPONSE

Flowonix Claim:

In addition to accuracy over the refill cycle the Prometra® Pump has lower variability at time points over the course of the refill cycle. This accuracy should provide patients with a more consistent therapeutic effect, potentially eliminating complaints from changes in prescribed therapy, including confusion, altered mental state, sleepiness, nausea, or lack of therapeutic effect near the end of the refill cycle.

- Full Pump
- 4,500 M Elevation
- 41° C Body Temp



- Includes a pump replacement which can't happen during a refill cycle (by definition of what a refill cycle is)

- Empty Pump
- Sea Level
- 33° C Body Temp

Medtronic Response:

- The result shown in the graph does not make sense. These results occur under extreme conditions that are highly unlikely to occur in the specified combinations and times. In addition the chart incorporates our Bench Accuracy Specification (pump to pump variability). Obviously there is no pump replacement during the refill cycle.[4]

	SynchroMed™ II	Prometra®
Clinical Accuracy* (average)	101%[2]	97%[1]
Average Bench Accuracy Average Range	 97.4%[3] ±7.5%	Data Not Provided in Labeling
Accuracy Specification (Bench Accuracy all pumps)	±14.5%[3]	Data Not Provided in Labeling
Day-to-day Repeatability	± 0.3%[4]	Data Not Provided in Labeling

*Based upon studies conducted for each product and as further reflected in each product's labeling. No clinical head-to-head studies have been performed comparing SynchroMed™ and Prometra®.

Flowonix labeling only reports clinical accuracy for the Prometra pump, not Prometra II.

Resource: ***Quality Demonstrated Sell Sheet***

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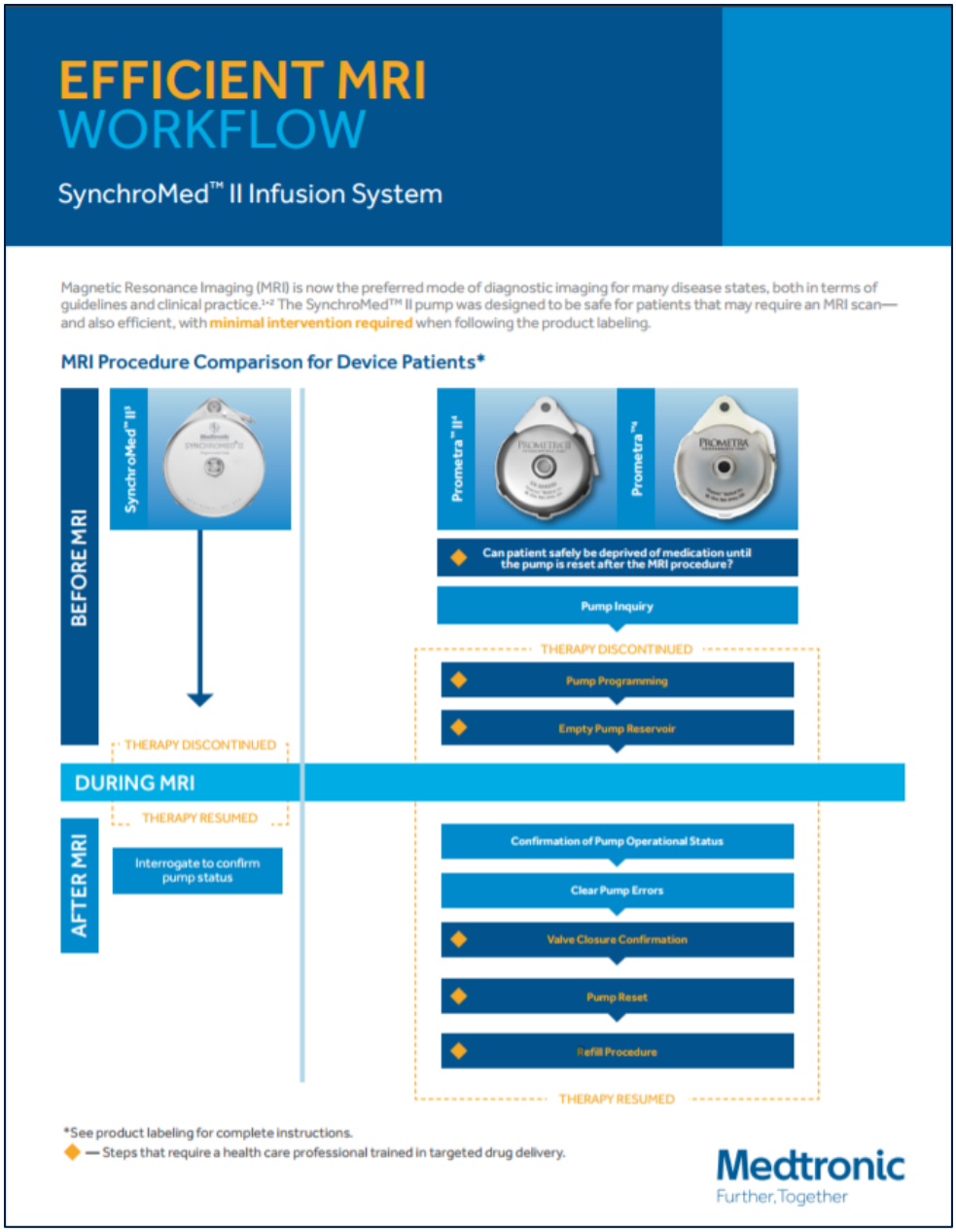
#3 MRI COMPARISON
MEDTRONIC RESPONSE

Medtronic Response: [1,5,6]

- Although Flowonix has added a valve to the pump, they have also added a significant level of complexity to the MRI process.
- 9 steps (6 which require HCP intervention) with Prometra® II vs 1 with SynchroMed™ II.



Resource: ***MRI Sell Sheet***

#4 COMMITMENT TO IMPROVING TDD
FLOWONIX CLAIM AND MEDTRONIC RESPONSE

Flowonix Claim:

Medtronic Response:

- Both products have labeling warnings for Inflammatory Mass (Granuloma). Right now*, Prometra® has reported cases in the MAUDE database for both granuloma and pocket fill.
- There are numerous confirmed Prometra® failures in the FDA MAUDE Database and the Flowonix response in many of them provided NO detail as to why the failures are happening*.
- We have failures in MAUDE as well, but we are transparent about our analysis. ***Medtronic actively tracks the performance of SynchroMed™ II***, while others use ***reactive device management*** and respond only when issues occur.
- Our extensive registry (over 7,000 active prospectively monitored SynchroMed™ II devices) provides visibility to how our pump performs.[7]
- ***Question: What clinical data can Flowonix provide?***

*October 2017

Resource: ***Quality Demonstrated Sell Sheet*** ***and*** ***Therapy Experience Sell Sheet***

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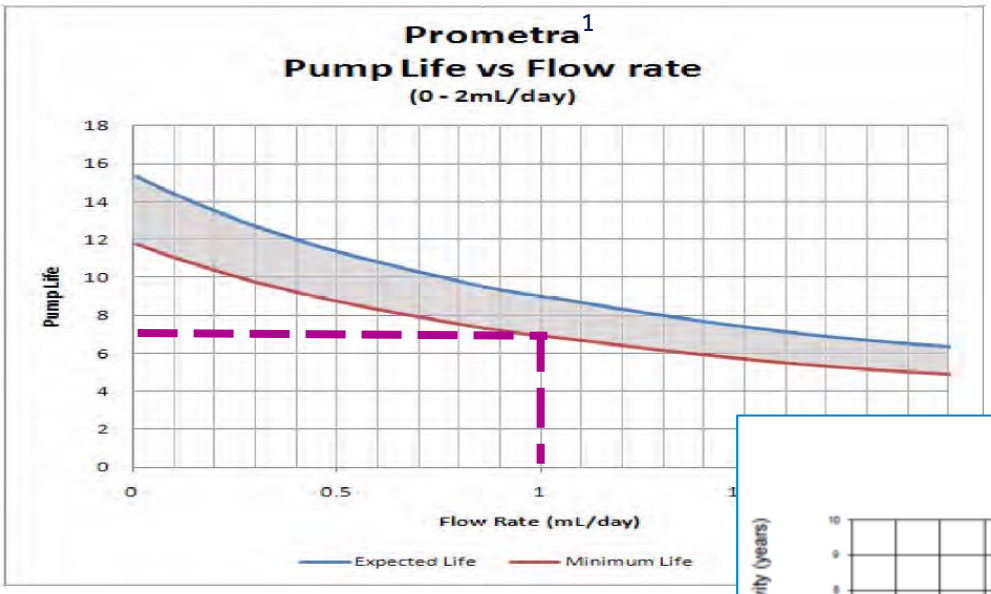
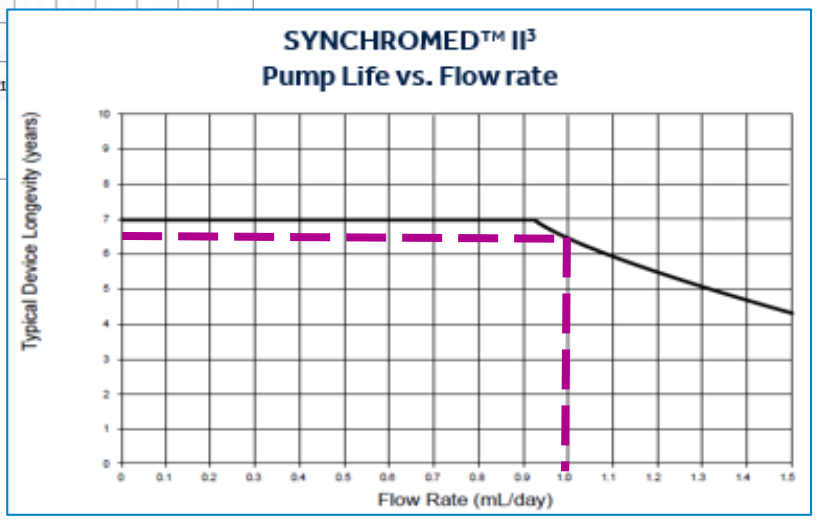
#5 DEVICE LONGEVITY
FLOWONIX CLAIM AND MEDTRONIC RESPONSE

Flowonix Claim:





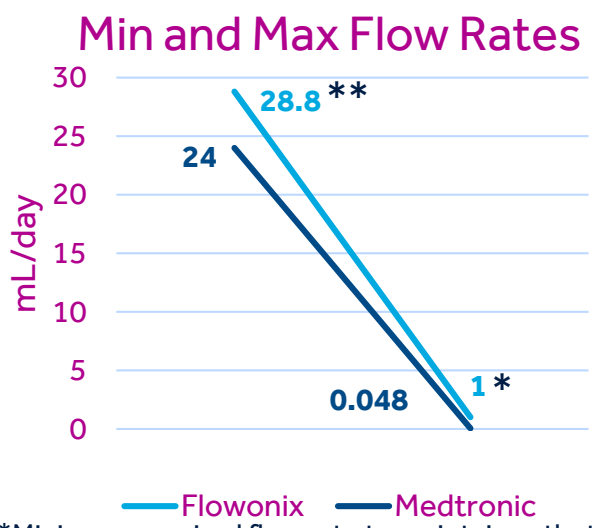
Medtronic Response:

- Prometra® labeling specifies a 10 year pump life at a 0.25 mL/day flow rate.
- Referring to the chart above**, Prometra® pump life is approximately 7 years at 1.0 mL/day flow rate.[1]**
- **SynchroMed™ II labeling specifies pump life is approximately 6.5 years at 1.0 mL/day flow rate.[3]**
- Based on our Product Performance Report, **97.2% of SynchroMed™ II pumps continued to perform when used with on-label drugs for pain at 75 months (6.25 years).[7]** Data in the report reflects real world flow rates.

#6 FLOW RATE
FLOWONIX CLAIM AND MEDTRONIC RESPONSE

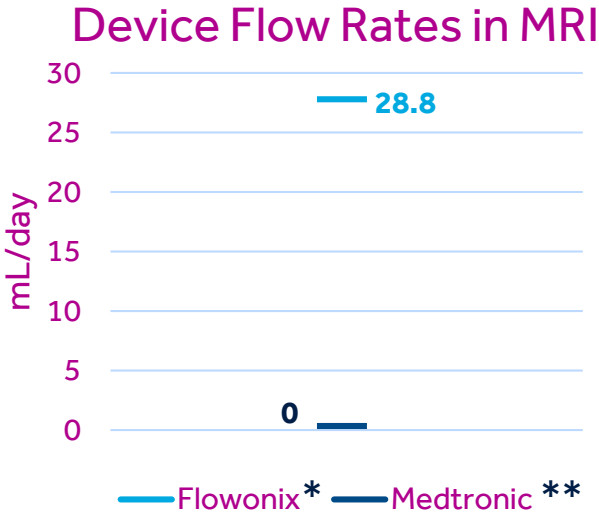
Flowonix Claim:

Flowonix pump technology is better setup for delivering low-dose TDD because it can provide a basal rate of zero and deliver therapy in bolus doses only with pulsatile flow[1] .



*Minimum required flow rate to maintain catheter patency

**28.8mL/day is based on accumulator volume



*Prometra I and II labeling require all drug be removed from pump reservoir prior to MRI to avoid inadvertent high flow rate delivery into intrathecal space.

**The Synchromed II motor stalls during the presence of an MRI .

Medtronic Response:
Using a bolus only dosing strategy is interesting but are there any clinical advantages over simple continuous or flex dosing?

- The Prometra II pump labeling states that in order to maintain catheter patency a flow rate of 1.0 mL/day or higher is required.
- The SynchroMed II pump labeling requires a minimum basal rate 0.048 mL/day (20x less than Prometra II).
- Using the CONTROL Workflow with drug concentrations of 0.5 mg/mL or 1mg/mL would result in basal rates of 0.001 mg/hour or 0.002 mg/hour, respectively.
- The basal rate of delivery at these concentrations represents a small fraction of recommended morphine dosing[9] and the difference between 0.002 mL/hr and 0 mL/hr would not be expected to impact the overall efficacy of the therapy.

FLOWONIX TARGETING
MEDTRONIC RESPONSE

Flowonix Target:
High Volume Medtronic TDD Customers

Medtronic Response:
- Nobody is more committed to TDD than Medtronic. With over 30 years experience and more than 400,000 pumps that have been implanted worldwide, we are the only company with long term dedication to TDD.[8]

Flowonix Target:
Patients due for replacement that have an old catheter (hooking Prometra® up to our old catheter and using our revision kit).

Medtronic Response:
- The Ascenda catheter blends more than 20 years of Medtronic infusion system expertise with the latest technology to provide confidence in uninterrupted therapy and reduced patient management burden.
- Use of the Prometra® pump with our catheter is off label.

Resource: ***Quality Demonstrated Sell Sheet*** ***and*** ***Therapy Experience Sell Sheet***

REFERENCES

1. Flowonix Medical Inc. Web Site. Prometra II Programmable Pump IFU http://www.flowonix.com/sites/default/files/pl-31790-03_-_prometra_ii_programmable_pump_ifu_us_commercial_-_final.pdf. Accessed October 2017.
2. SynchroMed Therapy Clinical Accuracy. http://manuals.medtronic.com/wcm/groups/mdtcom_sg/@emanuals/@era/@neuro/documents/documents/contrib_190054.pdf. Accessed March 2017.
3. Medtronic SynchroMed™ II Model 8637 Implant Manual, 2011.
4. Medtronic data on file. Engineering bench study that included >1,000 data points from 23 pumps. Typical infusion rates of 100, 300, 500 and 700 mcL/day were included under the following conditions: 37 degrees C, full, mid- and low-reservoir volumes, 300 meters above sea level. "Repeatability" is defined as the extent to which volumes delivered by the SynchroMed™ II Infusion System varied from refill to refill. June 2016.
5. MRI Information for SynchroMed II Pump. https://professional.medtronic.com/mri/surescan-mri-radiologists/dis/mri-pumps/index.htm#.WUKaOOsrLn8. Accessed June 2017.
6. Flowonix Medical Inc. Web Site. http://www.flowonix.com/sites/default/files/PL-21790-00%20-%20Prometra%20Programmable%20Pump%20IFU%20%28Flowonix%20-%20US%20Commercial%29.pdf. Accessed October 2017.
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8. Medtronic Data on File. October 2017.
9. Deer et al., 2017. The Polyanalgesic Consensus Conference (PACC): Recommendations on Intrathecal Drug Infusion Systems Best Practices and Guidelines. Neuromodulation 2017; E-pub ahead of print. DOI: 10.1111/ner.12538

Resource Links:
SynchoMed™ II Durable Design Update iPDF
Quality Demonstrated Sell Sheet
MRI Sell Sheet
Therapy Experience Sell Sheet

Accuracy Defined By Medtronic

Clinical Accuracy: Accuracy measured under clinical conditions for implanted pumps where aspirated volume (measured with a syringe) is compared to the expected volume provided by the pump (based on the programmed flow rate and the reservoir volume at the start of the refill cycle).
Bench Accuracy: Accuracy measured on a test bench where measured flow rate is compared to programmed flow rate.
Accuracy vs. Repeatability: Accuracy includes pump to pump and environmental variations while repeatability is the day to day precision of a particular pump under stable environmental conditions.
Accuracy Specification: Medtronic verifies through Bench Accuracy testing that all production manufactured pumps will fall within the Accuracy Specification.
Accuracy Average and Range: Each accuracy data set has both an average value and range of values.

SYNCHROMED™ II BRIEF STATEMENT

SynchroMed® II Drug Infusion System Brief Statement:

Product technical manuals and the appropriate drug labeling must be reviewed prior to use for detailed disclosure.

Indications: US: Chronic intrathecal infusion of Infumorph® preservative-free morphine sulfate sterile solution in the treatment of chronic intractable pain, Prialt® chronic intrathecal infusion of preservative-free ziconotide sterile solution for the management of severe chronic pain, and chronic intrathecal infusion of Lioresal® Intrathecal (baclofen injection) for the management of severe spasticity. Outside of US: Chronic infusion of drugs or fluids tested as compatible and listed in the product labeling.

Drug Information: Refer to appropriate drug labeling for indications, contraindications, warnings, precautions, dosage and administration, screening procedures, and under-/overdose symptoms and methods of management. Patients should be informed of the signs and symptoms of drug under- or overdose, appropriate drug warnings and precautions, and signs and symptoms that require medical attention.

Contraindications: System implant is contraindicated in the presence of an infection; implant depth greater than 2.5 cm below skin; insufficient body size; and spinal anomalies. Use of the system with drugs with preservatives and drug formulations with pH ≤3. Use of CAP kit for refills or of refill kit for catheter access and use of PTM to administer opioid to opioid-naïve patients or to administer ziconotide.

Warnings: Non-indicated formulations may contain neurotoxic preservatives, antimicrobials, or antioxidants, or may be incompatible with and damage the system. Failure to comply with all product instructions, including use of drugs or fluids not indicated for use with system, or of questionable sterility or quality, or use of non-Medtronic components or inappropriate kits, can result in improper use, technical errors, increased risks to patient, tissue damage, damage to the system requiring revision or replacement, and/or change in therapy, and may result in additional surgical procedures, a return of underlying symptoms, and/or a clinically significant or fatal drug under- or overdose.

An inflammatory mass that can result in serious neurological impairment, including paralysis, may occur at the tip of the implanted catheter. Clinicians should monitor patients carefully for any new neurological signs or symptoms, change in underlying symptoms, or need for rapid dose escalation. Monitor patients appropriately after refill if a pocket fill is suspected. Failure to recognize signs and symptoms of pocket fill and seek appropriate medical intervention can result in serious injury or death. Overinfusion may lead to underdose or overdose symptoms. Strong sources of electromagnetic interference (EMI), can negatively interact with the pump and cause heating of the implanted pump, system damage, or changes in pump operation or flow rate, that can result in patient injury from tissue heating, additional surgical procedures, a return of underlying symptoms, and/or a clinically significant or fatal drug underdose or overdose. The SynchroMed II system is MR Conditional; consult the labeling for MRI information.

Precautions: Monitor patients after pump or catheter replacement for signs of underdose/overdose. Infuse preservative-free saline at minimum flow rate if therapy is discontinued for an extended period of time to avoid system damage. EMI may interfere with programmer telemetry during pump programming sessions. EMI from the SynchroMed programmer may interfere with other active implanted devices (e.g., pacemaker, defibrillator, neurostimulator).

Adverse Events: In addition to procedure-related risks, the following may occur: pocket seroma; hematoma; erosion; infection; pump inversion; post-lumbar puncture risks (spinal headache); CSF leak and rare central nervous system pressure-related problems; radiculitis; arachnoiditis; spinal cord bleeding/damage; meningitis; neurological impairment (including paralysis) due to inflammatory mass; allergic response to implant materials; surgical replacement due to end of service life or component failure; loss of therapy, drug overdose, or inability to program the pump due to component failure; catheter complications resulting in tissue damage or loss of or change in therapy; potential serious adverse effects from catheter fragments in intrathecal space.

For full prescribing information, please call Medtronic at 1-800-328-0810 and/or consult Medtronic's website at www.medtronic.com

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Rev 0817