

Increased Risk of Motor Stall and Loss of or Change in Therapy with Unapproved Drug Formulations

Summary

Medtronic Neuromodulation has confirmed through engineering analyses that the use of unapproved drug formulations can increase the risk of pump motor stall due to corrosion in the SynchroMed infusion systems. Use of unapproved drugs or fluids can result in increased risks to the patient and permanent damage to the pump. This can lead to permanent pump stalls requiring surgical replacement and a loss or change in therapy, which may lead to a return of underlying symptoms, drug withdrawal symptoms, or a clinically significant or fatal drug underdose. Unapproved drug formulations include drugs not listed in the labeling including admixtures, compounded drugs, and unapproved drug concentrations. Labeling is provided with the pump and catheter systems. Additional copies of approved product labeling can be obtained from your Medtronic representative.

How Does Corrosion Damage Occur?

Corrosive agents (e.g. chloride ion, sulfate ion) originating from drug formulations can permeate through the internal pump tubing and initiate corrosion of internal components. Some factors that can increase the permeation rate of the corrosive agents in the drug formulation include hydrophobicity, degree of positive ionization, impurities, preservatives, pH adjustments, and concentrations adjustments. Permeation of corrosive agents originating from many unapproved drug formulations can occur at significantly higher rates than for approved drug formulations.

In addition to permeation, damage can occur as a result of a leak in the pump tube resulting in direct exposure of internal pump components to corrosive agents from the drug solution. The manufacturing process includes inspection of pump tubes to guard against leaks at the time of manufacturing.

Clinical Significance

Intermittent or permanent pump motor stalls may be reported as a loss or change in therapy, which may lead to a return of underlying symptoms, drug withdrawal symptoms, or a clinically significant or fatal drug underdose.

Confirmed Unapproved Drugs That Have Resulted in Permanent Pump Stalls

Through returned product analysis and in vitro testing, Medtronic Neuromodulation has confirmed that unapproved drugs and drug formulations that have caused pump damage resulting in pump motor stalls include, but are not limited to, the following:

- Compounded drugs, including some formulations of baclofen and morphine
- Admixtures for severe spasticity therapy containing baclofen with clonidine, and baclofen mixed with other drugs
- Admixtures for chronic pain therapy containing fentanyl and/or sufentanil, bupivacaine, clonidine, hydromorphone, morphine, and baclofen.

Other unapproved drug formulations may also cause pump damage resulting in pump motor stalls.

Incompatible Formulations with the Infusion System Pumps

Additives, unapproved concentrations, and admixture solutions may alter the material properties of the infusion system components and exhibit chemical properties that are not compatible with the infusion system. This could interfere with the safe and reliable performance of the infusion system. Examples of these include:

- Some antimicrobial preservatives and antioxidant preservatives are known to damage the SynchroMed EL and SynchroMed II infusion systems (e.g., sodium metabisulfite).
- Drug concentrations that require additives to maintain solubility may not be compatible with the infusion system.
- Admixture solutions may result in increased permeation rates of corrosive agents.
- Drug formulations with a $\text{pH} \leq 3$ are not compatible with the infusion system.
- Higher permeation rates are generally associated with hydrophobic drugs (e.g. fentanyl, bupivacaine).

Compatible Formulations with the Infusion System Pumps

Drug formulations specified in the pump labeling have been tested for compatibility and in-pump stability with the SynchroMed infusion systems. The product labeling contains precise specifications and controls (e.g., concentration, pH, and impurities) to clarify which drug formulations constitute approved versus unapproved drugs and drug concentrations.

In studies performed by Medtronic Neuromodulation, approved drug formulations have shown significantly lower chloride (a corrosive agent) permeation rates, whereas unapproved drug formulations have shown a wide range of chloride permeation rates, with some unapproved drug formulations showing a level of chloride permeation rates orders of magnitude higher than for approved drugs.

Conclusion

Use only those drugs and drug formulations for which the SynchroMed infusion system is approved to minimize the potential for damage to the internal pump components. The use of unapproved drug formulations can increase the risk of pump motor stall due to corrosion in the SynchroMed infusion systems. Be aware that even if an approved drug formulation is currently being used, previous use of an unapproved drug formulation in that pump may have already increased the risk of corrosion leading to a permanent motor stall.