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United States

Tools for Safe Patient Management

DRUG FORMULATIONS

Medtronic Neurological Drug Delivery Pumps

Model 8616/8617 SynchroMed® Implantable Pump
Model 8626/8627 SynchroMed® EL Implantable Pump
Model 8637 SynchroMed® II Implantable Pump
Model 8472 IsoMed® Implantable Pump

Purpose

This Educational Brief provides important information for all Medtronic Neurological drug delivery infusion system pumps. This communication has two purposes:

- 1) To provide information about intraspinal drug formulations containing preservatives that may be neurotoxic; and
- 2) To provide information about drug formulations containing preservatives that may compromise the safe and effective performance of Neurological infusion system pumps.

Explanation of the Issue

Neurotoxic Formulations

According to the United States Pharmacopeia (USP) and European Pharmacopeia (EP), injections intended for intrathecal or epidural use may contain sodium chloride as a tonicity-adjusting agent, but they should not contain any other added additives. An injection that is free of both antioxidant preservative agents and antimicrobial preservative agents prominently bears on its label the words "preservative-free." In contrast, a commercial injection that contains either antioxidant preservatives or antimicrobial preservatives should be clearly labeled with the statement that it is not for intrathecal or epidural use since these agents are toxic to the central nervous system.^{1 - 2}

While this list is not exhaustive, alcohol, phenol, formaldehyde, and sodium metabisulfite are examples of additives that have been identified as neurotoxic.³ Additionally research on intraspinal analgesic infusion agents has highlighted the importance of maintaining pH in ranges of 4-8.⁴

Incompatible Formulations with Infusion System Pumps

The use of pharmaceutical products that are not specifically labeled for intraspinal administration via continuous infusion may cause damage to components of the Neurological drug infusion pumps. This could potentially jeopardize patient safety as a result of diminished device performance or device failure.

Do not use any solutions that contain antimicrobial preservatives or antioxidants. These additives may alter the material properties of the infusion system components or exhibit chemical properties that are not compatible with the infusion system. Additionally, some drug formulations may exhibit unexpected pH-dependent interactions with pump materials, thus extreme pH conditions could interfere with the safe and reliable performance of the infusion system.⁵

Recommendations for Patient Management

As you prescribe medications for administration using the Medtronic Neurological infusion systems, always:

- Refer to the appropriate drug information for a complete list of indications, contraindications, warnings, precautions, dosage and administration information.
- Ensure that the drug is preservative-free, and does not contain any antioxidant or antimicrobial agents.
- Ensure that the drug does not contain ethanol, and is within the pH range of 4-8.
- Contact your drug supplier, if you have questions about other excipients,.
- Consult the appropriate Pump Technical Manual for drug stability information.

Drug products specifically labeled for intraspinal administration via continuous infusion have undergone rigorous testing to ensure that the drug will not impact the operation of the device and that the device materials will not affect the quality of the drug.

Drugs approved for intrathecal and/or epidural use with some or all Neurological drug infusion pumps, for the treatment of chronic intractable pain or the management of severe spasticity, are listed below.

- Preservative-free morphine sulfate sterile solution
- Prial[®] (ziconotide intrathecal infusion)
- Lioresal[®] Intrathecal (baclofen injection)

If you suspect use of an incompatible solution Medtronic recommends contacting your drug supplier regarding the specific prescription.

If incompatible solution is confirmed, refer to the proper Medtronic product labeling for instructions on changing pump medications and, as always, continue to monitor the patient closely for the possible return of baseline symptoms that may indicate infusion system damage.

For Assistance

Contact Medtronic Technical Services: 1-800-707-0933.

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¹ The United States Pharmacopeia 28/National Formulary 23, Rockville,, MD, USP Convention Inc, 2004

² European Pharmacopeia, 4th Edition, Council of Europe, France, 2001

³ Gianino J, et al. Intrathecal Drug Therapy for Spasticity and Pain. Practical Patient Management. New York: Springer-Verlag, 1996.

⁴ Grouls RJE, Korsten EHM, Yaksh TL. General considerations in the formulation of drugs for spinal delivery. In Yaksh TL, ed. Spinal Drug Delivery. Amsterdam: Elsevier, 1999:371-393.

⁵ Bennett G, Deer T, Du Pen S, Rauck R, Yaksh TL Hassenbusch SJ. Future directions in the management of pain by intraspinal drug delivery. J Pain Symptom Manage 2000;20:S44-S50.