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A Company of the Fresenius Kabi Group

July 15, 2010

Dear Health Care Professional,

APP Pharmaceuticals ("APP") would like to inform you of important new prescribing information for injectable local anesthetics marketed by APP and other pharmaceutical companies. These local anesthetics include bupivacaine, ropivacaine, lidocaine, mepivacaine, and chloroprocaine—marketed by APP, respectively, as Sensorcaine®, Naropin®, Xylocaine®, Polocaine®, and Nesacaine®.[1] The new information concerns recent reports of chondrolysis (degeneration of cartilage) in patients given continuous intra-articular infusions of local anesthetics with elastomeric infusion devices to control post-surgical pain. The approved drug labels for local anesthetics do not include an indication for continuous intra-articular postoperative infusions or use of infusion devices, such as elastomeric pumps. Similarly, the FDA has not cleared any infusion devices with an indication for use in intra-articular infusion of local anesthetics.

The reports of chondrolysis involve primarily the glenohumeral (shoulder) joint. The local anesthetics (with and without epinephrine) were infused for extended periods of time (48 to 72 hours) directly into the intra-articular space using an elastomeric pump. In the majority of reported cases, the local anesthetic infused was bupivacaine with or without epinephrine. The causes of chondrolysis have not been determined, and the etiology is likely multifactorial. It is not known which specific factor or combination of factors contributes to the development of chondrolysis.

Working with the FDA, APP is updating its local anesthetic labels with the following information:

- WARNINGS

  Intra-articular infusions of local anesthetics following arthroscopic and other surgical procedures is an unapproved use, and there have been post marketing reports of chondrolysis in patients receiving such infusions. The majority of reported cases of chondrolysis have involved the shoulder joint; cases of glenohumeral chondrolysis have been described in pediatric and adult patients following intra-articular infusions of local anesthetics with and without epinephrine for periods of 48 to 72 hours. There is insufficient information to determine whether shorter infusion periods are not associated with these findings. The time of onset of symptoms, such as joint pain, stiffness and loss of motion can be variable, but may begin as early as the 2nd month after surgery. Currently, there is no effective treatment for chondrolysis; patients who experienced chondrolysis have required additional diagnostic and therapeutic procedures and some required arthroplasty or shoulder replacement.

[1]The new information also applies to procaine, although APP does not market this product. For more information, please see the FDA website at: http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm190302.htm.

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- DOSAGE AND ADMINISTRATION

  There have been adverse event reports of chondrolysis in patients receiving intra-articular infusions of local anesthetics following arthroscopic and other surgical procedures. [bupivacaine, ropivacaine, lidocaine, mepivacaine, or chloroprocaine] is not approved for this use (see WARNINGS and DOSAGE and ADMINISTRATION).

If you have any questions regarding this important prescribing information, please contact APP's Medical Affairs Department toll free at 1-800-551-7176 or fax a letter to 1-847-413-8571. You may also submit any adverse event information to those APP numbers or directly contact the FDA's MedWatch program at 1-800-FDA-1088 (telephone), 1-800-FDA-0178 (fax), or submit a report online at https://www.accessdata.fda.gov/scripts/medwatch/medwatch-online.htm.

Sincerely,

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