

## Drugs

### **Information for Healthcare Professionals - Chondrolysis Reported with Continuously Infused Local Anesthetics (marketed as bupivacaine, chlorprocaine, lidocaine, mepivacaine, procaine and ropivacaine)**

**[November 13, 2009 Updated: January 8, 2010]: The Food and Drug Administration (FDA) has reviewed 35 reports of chondrolysis (necrosis and destruction of cartilage) in patients given continuous intra-articular infusions of local anesthetics with elastomeric infusion devices to control post-surgical pain. The significance of this injury to otherwise healthy young adults warrants notification to health care professionals.**

**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.**

**Chondrolysis was diagnosed within a median of 8.5 months after the infusion. Almost all of the reported cases of chondrolysis (97%) occurred following shoulder surgeries. Joint pain, stiffness, and loss of motion were reported as early as the second month after receiving the infusion. In more than half of these reports, the patients required additional surgery, including arthroscopy or arthroplasty (joint replacement).**

**It is not known which specific factor or combination of factors contributed to the development of chondrolysis in these cases. The infused local anesthetic drugs, the device materials, and/or other sources may have resulted in the development of chondrolysis. It is important to note that single intra-articular injections of local anesthetics in orthopedic procedures have been used for many years without any reported occurrence of chondrolysis.**

**Local anesthetics are approved as injections for the production of local or regional anesthesia or analgesia. 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. The FDA has not cleared any infusion devices with an indication for use in intra-articular infusion of local anesthetics.**

**Health care professionals are encouraged to follow the instructions for use of elastomeric infusion devices, and to not use these devices for continuous intra-articular infusion of local anesthetics after orthopedic surgery.**

**Based on the reported cases of chondrolysis, following continuous intra-articular infusion with local anesthetics, the FDA is requiring the drug manufacturers to update their product labels to warn healthcare professionals about this potential serious adverse effect. FDA is also exploring possible options for addressing the safety issues with the infusion devices (e.g., labeling changes, etc.).**

The FDA is requiring the changes to the drug label under the authorities granted by the Food and Drug Administration Amendments Act (FDAAA) of 2007.

*This information reflects FDA's current analysis of data available to FDA concerning this drug. FDA intends to update this sheet when additional information or analyses become available.*

*To report any unexpected adverse or serious events associated with the use of this drug, please contact the FDA MedWatch program using the information at the bottom of the page.*

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## **Considerations for Health Care Professionals**

- Understand that both the local anesthetics and the elastomeric infusion devices—or any other type of device used for intra-articular infusions—are not approved or cleared by the FDA for continuous intra-articular infusion.
- Be aware of the possibility for and monitor for the emergence of the signs and symptoms of chondrolysis, such as joint pain, stiffness and loss of motion. The appearance of these symptoms can be variable, but they may begin two or more months after surgery.
- Recognize that patients experiencing chondrolysis may require additional diagnostic and therapeutic procedures and may eventually require arthroplasty (joint replacement).
- Inform patients of the signs and symptoms of chondrolysis so they are aware of and able to notify their healthcare professional if they experience persistent joint pain, stiffness, or a severe decrease or loss of motion in the joint.

## **Information for Patients**

- Discuss with your healthcare professional any questions or concerns you have about your orthopedic surgical procedure and what to expect immediately following surgery, including how to manage postsurgical pain.
- Talk with your healthcare professional about available FDA-approved options to manage postsurgical pain.
- If, after an orthopedic surgical procedure, you have received a prolonged infusion of a local anesthetic into your joint with a disposable elastomeric

pump or any other infusion pump, pay attention to symptoms of joint pain, stiffness and a decrease or loss of motion and alert your healthcare professional if these symptoms persist.

## Data Summary

Between 2006 and 2008, 35 reports of chondrolysis (primarily in the shoulder) occurring in patients administered continuous intra-articular infusions of local anesthetics with elastomeric infusion devices were reported to the FDA's Adverse Event Reporting System (AERS). Thirty-two (91%) of these patients received bupivacaine (with or without epinephrine) as an intra-articular infusion after having undergone arthroscopic and other surgical procedures.<sup>1</sup> Two of the 32 patients received ropivacaine in addition to bupivacaine. Additionally, two of the 35 patients received bupivacaine as a single injection along with an intra-articular infusion of lidocaine. The average infusion time in the reported cases was between 48 and 72 hours. The most commonly reported site of infusion was the glenohumeral (glenoid) space (46%).

Sixteen of the 32 (50%) bupivacaine-associated AERS reports included the dose administered, with 10 of 16 patients receiving 500mg over 48 hours or 250mg/day. While this daily intra-articular dose was within the maximum dose listed in the drug label (400mg/day), it is important to note that this maximum labeled daily dose was determined for the approved uses and not for off-label uses such as continuous intra-articular infusions with elastomeric infusion devices.

In the reported cases, symptoms of chondrolysis occurred as early as 2 months after the infusion (median of 5 months) and chondrolysis was diagnosed with a median of 8.5 months after the infusion. The median age of the affected patients was 25 years, with an age range of 16-58 years. Six of the reports involved pediatric patients between 16 and 18 years. In almost all of the reported cases (34/35 or 97%), the location of chondrolysis was in the shoulder joint. The remaining report involved the knee joint.

The FDA received four additional reports of chondrolysis in patients administered continuous intra-articular infusions of lidocaine in the shoulder after the initial 35 bupivacaine-related cases reported from 2006 to 2008.<sup>2</sup> The FDA AERS data is supported by recent literature reports of patients experiencing chondrolysis after bupivacaine infusions and preclinical studies showing chondrolysis after chondrocyte exposure to bupivacaine, lidocaine, and ropivacaine.<sup>3,4,5,6</sup>

The most common manufacturer of elastomeric infusion device mentioned among the 32 infusion-patients was Stryker (n=11). The other companies mentioned in the report were the manufacturers I-Flow and Breg, and the distributor Don Joy (n=14 combined). This finding suggests that the reported cases of chondrolysis are not associated with any single manufacturer of elastomeric infusion devices.

Based on the reported cases of chondrolysis following continuous intra-articular infusion of local anesthetics with elastomeric infusion devices, the FDA is requiring the manufacturers of local anesthetics and of pumps that may be used to infuse local anesthetics to update their product labels to warn healthcare professionals about this potential serious adverse effect. FDA is also exploring possible options for addressing the safety issues with the infusion devices (e.g., labeling changes, etc.). Because the reported cases involved significant injury to otherwise healthy young adults, FDA wants to advise healthcare professionals that elastomeric infusion devices or any other infusion pump are not cleared by FDA to deliver intra-articular infusions of local anesthetics and should not be used for this purpose.

### **References:**

<sup>1</sup>The 35 cases were obtained from an AERS search for *bupivacaine reports* received on or before 7/16/08.

<sup>2</sup> These 4 reports are from an additional AERS search for reports of *local anesthetics other than bupivacaine* received up to 1/22/09.

<sup>3</sup>Baillie DS, Ellenbecker TS. Severe chondrolysis after shoulder arthroscopy: a case series. *J. Shoulder Elbow Surg.* 2009; 18:742-747.

<sup>4</sup>Hansen BP, Beck CL, Beck EP, Townsley RW. Postroscopic glenohumeral chondrolysis. *Am. J. Sports. Med.* 2007; 35:1628-1634.

<sup>5</sup>Dragoo JL, Kortokova T, Kanwar R, Wood B. The effect of local anesthetics administered via pain pump on chondrocyte viability. *Am. J. Sports. Med.* 2008; 36:1484:1488.

<sup>6</sup>Piper SL, Kim HT. Comparison of ropivacaine and bupivacaine toxicity in human articular chondrocytes. *J. Bone Joint Surg.* 2008; 90:986-991.

## **Related Information**

- [Infused Local Anesthetics Information](#)

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