

# Lumiracoxib (Prexige<sup>®</sup>) and Hepatotoxicity

## What is Lumiracoxib (Prexige<sup>®</sup>)

- A new COX-2 inhibitor / NSAID indicated in Canada for the treatment of osteoarthritis

## Why have the Australians removed Prexige<sup>®</sup> from their market?

- EIGHT cases of severe hepatitis have been reported in Australian patients since spring 2007
- Two of these patients have died and two have required a liver transplant
- **All cases appear to have occurred at doses of 200-400mg/day of Prexige (the maximum dose approved for use in Canada is 100mg/day; higher doses were the “norm” in Australia)**

## Is this a KNOWN side effect of Prexige<sup>®</sup>?

- ↑LFTs was noted in the **TARGET** trial<sup>1</sup> and in the Health Canada *Summary Basis of Decision*<sup>2</sup>
  - **100mg/day** dose: **0.9%** had ALT ↑ >3X normal levels after 12 months
  - **200–400mg/day** doses: **2.2 - 2.6%** had ALT ↑ >3X normal levels after 12 months
    - Note: the absolute risk increase of ≥1.3% seen in this trial results in an **NNH = <77**
      - For every 77 patients treated, with >100mg/day lumiracoxib there was 1 extra case of ALT elevation >3x normal at 1 year (The overall GI benefit in TARGET resulted in an **NNT = 119**)

## What is Health Canada doing about this?

- Health Canada has released an advisory on the topic, stating that they are continuing to assess data submitted by the manufacturer, but have made no decision to restrict it's sale in Canada<sup>3</sup>

## What should YOU do about this?

### In General:

- Consider starting with regular dosing of acetaminophen in osteoarthritis management as per existing guidelines
- Remember that all NSAIDs/COXIBs have potential risks that warrant caution, and sometimes contraindication in patients with gastrointestinal, cardiovascular, renal and hepatic disease
  - Compared to NSAID monotherapy, a “traditional NSAID + PPI” or “COXIB monotherapy” will reduce GI risk only modestly. There are many potential confounding variables in assessing both GI and overall patient risk.
  - Diclofenac 75mg BID was associated with a 4% incidence of elevated AST in the CLASS trial.

### For lumiracoxib (Prexige):

- Avoid doses > 100mg/day
- Stop drug if persistent AST/ALT elevations or signs of hepatotoxicity (e.g. jaundice, dark urine, malaise, anorexia)
- Avoid in patients with pre-existing liver dysfunction or active liver disease
- It is unclear how frequent AST/ALT should be monitored in patients taking lumiracoxib chronically. Onset of severe hepatitis may be too sudden to make AST/ALT monitoring useful.

**Update Oct/07:** Health Canada **removes** Prexige from the Canadian market after reviewing the above information, **PLUS** becoming aware of 4 new (2 are new Canadian cases) of severe hepatitis occurring at only the 100mg/day dose.<sup>4</sup>

Originally prepared for *Rapid Rx* - Aug 21/07 by Derek Jorgenson, PharmD;  
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RxFiles NSAIDs, COXIBs & Other Analgesics Chart: <https://www.rxfiles.ca/acrobat/CHT-NSAID-Cox2.pdf>



<sup>1</sup> a) Farkouh ME, Kirshner H, Harrington RA. Comparison of lumiracoxib with naproxen and ibuprofen in the Therapeutic Arthritis Research and Gastrointestinal Event Trial (**TARGET**), cardiovascular outcomes: randomised controlled trial. *Lancet* 2004;364:675-84.

b) Schnitzer TJ, Burmester GR, Mysler E., Comparison of lumiracoxib with naproxen and ibuprofen in the Therapeutic Arthritis Research and Gastrointestinal Event Trial (**TARGET**), reduction in ulcer complications: randomised controlled trial. *Lancet* 2004;364:665-74.

<sup>2</sup> Health Canada decision: [http://www.he-sc.gc.ca/dhp-mps/prodpharma/sbd-smd/phase1-decision/drug-med/sbd\\_smd\\_2007\\_prexige\\_102465\\_e.html](http://www.he-sc.gc.ca/dhp-mps/prodpharma/sbd-smd/phase1-decision/drug-med/sbd_smd_2007_prexige_102465_e.html)

<sup>3</sup> Health Canada advisory - lumiracoxib. [http://www.he-sc.gc.ca/ahc-asc/media/advisories-avis/2007/2007\\_102\\_e.html](http://www.he-sc.gc.ca/ahc-asc/media/advisories-avis/2007/2007_102_e.html)

<sup>4</sup> Health Canada advisory- lumiracoxib Oct/07 [http://www.he-sc.gc.ca/ahc-asc/media/advisories-avis/2007/2007\\_141\\_e.html](http://www.he-sc.gc.ca/ahc-asc/media/advisories-avis/2007/2007_141_e.html)