Lumiracoxib (Prexige©) and Hepatotoxicity

What is Lumiracoxib (Prexige©)

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

Why have the Australians removed Prexige© 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©?

- ↑LFTs was noted in the TARGET trial¹ and in the Health Canada Summary Basis of Decision ²
  - 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 Canada³

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. ⁴

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