### Emerging Drug List

**VALDECOXIB**

#### Generic (Trade Name): Valdecoxib (Bextra®)

#### Manufacturer: Pharmacia Inc. and Pfizer (co-marketers)

#### Indication:
For the treatment of the signs and symptoms of osteoarthritis, adult rheumatoid arthritis and primary dysmenorrhea. At this date, it has not yet been approved for use in acute pain although this indication was sought when it was originally submitted for review.

#### Current Regulatory Status:
Bextra was approved in the U.S. by the FDA in November 2001 and was subsequently marketed. In Canada the regulatory status of this agent is unknown.

#### Description:
Valdecoxib is a NSAID with relative selectivity for the cyclooxygenase (COX)-2 enzyme. After oral administration, its approximate bioavailability is 83 per cent, and it reaches a maximum concentration in three hours. It is highly protein bound (98 per cent), and has a half-life of 8.1 hours. Similar to celecoxib, it too is a sulfonamide derivative. The advocated dosage for the above mentioned indications is 10 mg daily, with the exception being dysmenorrhea where 20 mg bid as needed can be used.

#### Current Treatments:
Older NSAIDs include diclofenac salts (Voltaren® - Novartis), etodolac (Ultradol® - P&G), indomethacin (Indocid® - Merck), ketorolac tromethamine (Toradol® - Hoffman LaRoche), sulindac (generics), mefenamic acid (Ponstan® - Pfizer), piroxicam (Feldene® - Pfizer), tenoxicam (generics), fenoprofen (Nalfon® - Eli Lilly), flurbiprofen (Ansaid® - Pharmacia), ibuprofen (Motrin® - McNeil), ketoprofen (Orudis® - Aventis), naproxen (Naprosyn® - Hoffman LaRoche, oxaprozin (Daypro® - Pharmacia), tiaprofenic acid (Surgam® - Aventis), nabumetone (Relafen® - GSK), choline magnesium trisalicylate (Trilisate®), and diflusinal (generics). Newer NSAID with relative cox-2 selectivity include rofecoxib (Vioxx® - Merck), celecoxib (Celebrex® - Pharmacia) and meloxicam (Mobicox® - Boehringer Ingelheim).

#### Cost:
As this product is not yet available in Canada, no Canadian price is available at this time. In the U.S., Bextra® is available as 10 and 20 mg tablets; an online pharmacy was quoting a cost of $2.49-$2.62 per tablet.

#### Evidence:
Although very little published evidence is available, a "New Drug Application" report on the web site the Food and Drug Administration describes randomized controlled trial data of valdecoxib in dysmenorrhea (n=2), osteoarthritis (n=8), and rheumatoid arthritis (n=5). Trials of valdecoxib in other acute pain conditions have been conducted but the results are not available from the FDA report. The evidence suggests valdecoxib does not appear to have advantages in efficacy when
compared with: (1) naproxen in dysmenorrhea studies; (2) ibuprofen or diclofenac in osteoarthritis studies; or (3) naproxen in rheumatoid arthritis studies.

The evidence surrounding the safety of valdecoxib compared to standard NSAIDs is less unambiguous. Although several studies were conducted to assess safety, concerns about the lack of power to detect clinically significant events led one FDA reviewer to conclude "a rigorous assessment of the overall comparative safety on valdecoxib versus less selective NSAIDs would require a large clinical outcome study." Because of this, the standard warning applied to all NSAIDs, describing the increased risk of GI ulceration, bleeding and perforation, can be observed on the U.S. FDA product monograph. Concerns relating to the increased incidence of edema and hypertension (compared to standard NSAIDs) in the elderly in doses outside the recommended 10 mg daily are also outlined in the document.

Commentary:

Like other pipeline coxibs, in vitro data suggests this agent is more selective than those currently marketed in Canada; whether this has an important clinical effect will require further study. An increased incidence of serious adverse events, including heart attack and thrombosis, have been observed in larger proportions of patients taking the most selective coxib currently available compared with naproxen. The reason why more selective inhibitors of COX-2 may pose a health risk has been discussed by Mukherjee.

Even without defining a clear niche for this new class of agents, the availability of newer entities has not detracted from its predecessors. According to Pfizer's first quarter earning release, its two agents (celebrex and valdecoxib) currently account for approximately 22 per cent of the weekly new prescriptions relative to the NSAID market. The advent of valdecoxib is not compromising the strength of celecoxib sales; despite valdecoxib's launch, celecoxib's share of new prescriptions (weekly) has increased by 19 per cent.

References:


