Therapeutic Trends

Managing Arthritic Pain

Insight and Outlook from IMS Health

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Osteoarthritis (OA) is the most common form of arthritis, affecting three million Canadians (one in 10).[1] Rheumatoid arthritis (RA) is less common, affecting about 300,000 Canadians (one in 100).[1] Two-thirds of those with arthritis are women and nearly 60% are under the age of 65.[1] The most common effects of long-term arthritis are chronic pain and reduced mobility.[1] The treatment of musculoskeletal diseases (arthritis and osteoporosis) costs Canadians $16.4 billion every year, the second costliest after heart disease.[1]

OA is a degenerative joint disease that usually affects hands and weight-bearing joints.[2] It results from the breakdown of cartilage. RA is a chronic autoimmune disorder that causes inflammation and deformation of the articulations, most commonly hands and feet, but it can also affect internal organs such as the eyes, lungs or heart.[2] It is estimated that 10% of hospital admissions in Canada are associated with arthritis.[2]

TREATMENT OPTIONS

According to the Canadian Consensus Conference (CCC),[3] NSAIDs are the drug of choice for patients with moderate-to-severe OA while acetaminophen can be considered primary therapy in mild OA and as adjunct therapy in moderate or severe cases.[3] For patients with risk factors such as peptic ulcer disease (including perforation, ulcer, bleed) the CCC recommends COX-2 inhibitors as first-line therapy.[3] In patients with a history of an upper GI bleed in the preceding four to six weeks, the guidelines suggest proton pump inhibitors (PPIs) or misoprostol to be

Table 1
Top 10 recommended molecules by Canadian office-based physicians for OA and RA in 2006

Top 10 Molecules (OA)	Class	Top 10 Molecules (RA)	Class
1. Acetaminophen	Analgesic	1. Methotrexate	DMARD
2. Celecoxib	COX-2	2. Hydroxychloroquine	DMARD
3. Diclofenac	NSAID	3. Folic acid	
4. Naproxen	NSAID	4. Prednisone	Corticosteroid
5. Diclofenac with Misoprostol	NSAID	5. Celecoxib	COX-2
6. Methylprednisolone	Corticosteroid	6. Leflunomide	DMARD
7. Acetaminophen with codeine	Analgesic with opioid	7. Naproxen	NSAID
8. Meloxicam	COX-2	8. Gold sodium thiomalate	DMARD
9. Ibuprofen	NSAID	9. Etanercept	Biol. Resp. Mod.
10. Acetaminophen with oxycodone	Analgesic with opioid	10. Methylprednisolone	Corticosteroid

OA: Osteoarthritis RA: Rheumatoid arthritis DMARD: Disease-Modifying Anti-Rheumatic Drug
Source: IMS Health Canada, Canadian Disease and Therapeutic Index.

co-administered. The guidelines also state that COX-2 inhibitors be selected over non-specific NSAIDs in patients on anticoagulants.[3]

For RA, the American College of Rheumatology Subcommittee on Rheumatoid Arthritis Guidelines[6] state treatment must be tailored to the individual and often include to start the therapy with a disease-modifying anti-rheumatic drug (DMARD) such as methotrexate, hydrochloroquine and sulfasalazine. NSAIDs, glucocorticoid joint injection and/or low-dose prednisone may be considered to alleviate symptoms, if necessary.[4,6] Recent studies have shown the most aggressive treatment for controlling RA may be a combination of methotrexate plus another drug, particularly a biological response modifier, such as Remicade®.[4,5] Enbrel® (etanercept) is the first biological response modifier to receive Health Canada approval for patients with moderate-to-severe RA.[7]

THE MOST COMMONLY USED DRUGS

Table 1 shows the most commonly recommended drugs for OA and RA by Canadian office-based physicians. For OA, acetaminophen is most often recommended, followed by celecoxib, then diclofenac and naproxen. For RA, the most commonly recommended therapies include methotrexate, followed by hydroxychloroquine (both DMARDs) and folic acid. It is suggested that patients take folic acid supplements along with methotrexate to prevent its side-effects.[8]

COX-2 INHIBITORS

These drugs were first marketed in 1999 as anti-inflammatory agents that caused fewer GI side-effects, due to the fact that they blocked the COX-2 enzyme that promotes joint inflammation while sparing a similar enzyme, COX-1, which helps protect the mucous lining in the stomach. COX-2s are generally indicated for RA, OA and primary dysmenorrhea.

On September 30, 2004, Vioxx® was withdrawn from the market based on new safety information showing a possible increased risk of cardiovascular events. A few months later, on December 17, 2004, another popular COX-2, Celebrex® (celecoxib), was the subject of a drug advisory warning issued by its manufacturer. The warning also cited increased risk of heart problems. Bextra®, another COX-2, was taken off the market in April 2005.[9] Prexige® is the first new COX-2 to be approved in Canada since that time.

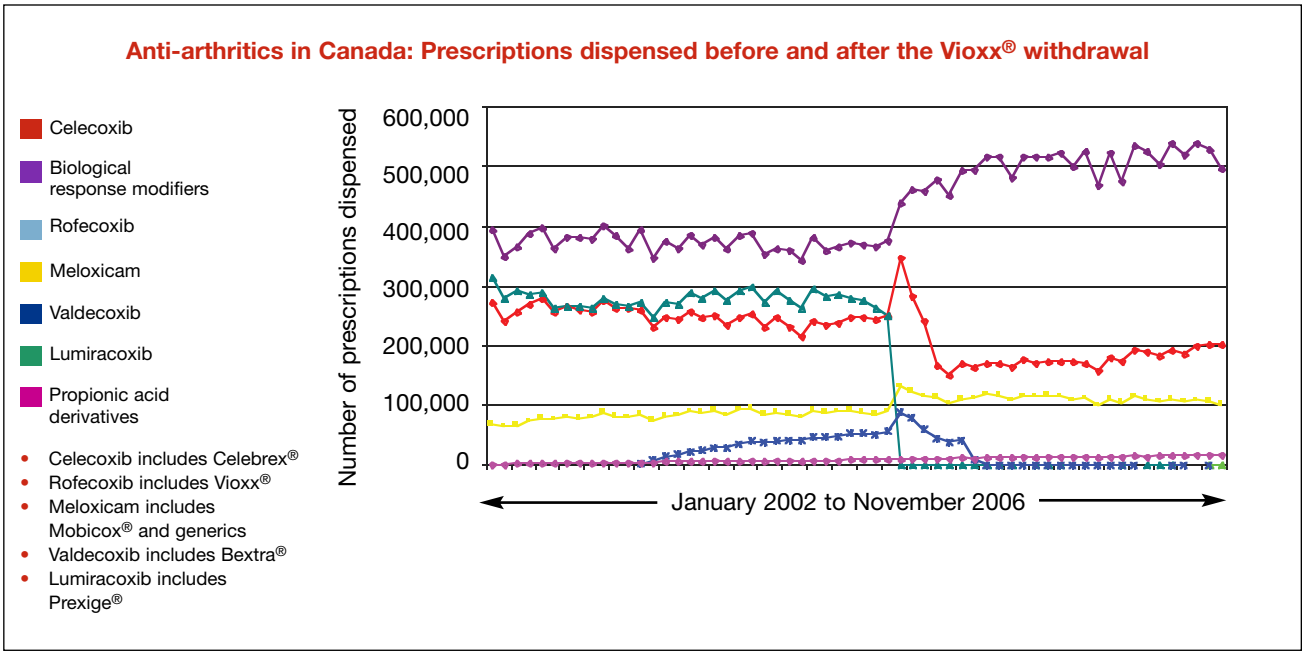

Figure 1. Anti-arthritics in Canada: Prescriptions dispensed before and after the Vioxx® withdrawal.
Source: IMS Health Canada, Canadian CompuScript Audits.

HOW THE MARKET HAS CHANGED

Figure 1 illustrates the anti-arthritic prescription market in Canada before and after the Vioxx® withdrawal. Prescriptions for celecoxib increased immediately following the Vioxx® withdrawal, subsequently falling sharply before levelling off in May 2005; celecoxib prescriptions have been slowly increasing since that time. Prescriptions for meloxicam and propionic acid derivatives (NSAIDs) have increased slightly since the end of 2004. Biological response modifiers (BRMs) represent a new and promising alternative for RA therapy and, due to their high cost, are generally only approved for treatment following failure of other therapies (DMARDs and NSAIDs). Prescriptions for BRMs grew by an average of 44% from 2002 to 2006 but their share of the anti-arthritic market in 2006 was only 1.6%.

THE SHIFT TO OTC

What the charts and graphs do not show is the extent of the shift from prescription medications to over the counter (OTC) drugs, including acetaminophen and ibuprofen. Results from our analysis up to June 2007 show that Tylenol® Extra Strength has the third largest share in drug recommendations for OA treatment.[10] In 2004, it ranked fifth. CPM

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