# Reaching and influencing consumers in the prescription medicine market

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**Abstract**

**Purpose** – Celebrex became the first of a new class of drugs known as COX-2 selective non-steroidal anti-inflammatory drugs. It improves treatment for arthritis sufferers without compromising the protective lining of the stomach. The purpose of this paper is to illustrate how direct-to-consumer advertising (DTCA) of prescription medicines can be used to rebuild faith in the cyclooxygenase-2 (COX-2) product category.

**Design/methodology/approach** – The case is developed using published sources and no input is required from company representatives. The presentation style follows the classic comprehensive case format used in postgraduate teaching programmes.

**Findings** – Business executives and strategic marketing students would benefit from a discussion on how external environmental factors can suddenly impose a review of marketing strategy. The reader learns how management addresses the business dilemma using DTCA.

**Research limitations/implications** – A blockbuster rival drug Vioxx is withdrawn due to cardiovascular (CV) health safety concerns. A resulting dominant market situation soon becomes a business dilemma. The Federal Drug Administration calls for a “black box” warning label on Celebrex, the most serious type of warning.

**Practical implications** – The implications are that having a product in a class of its own is not enough. It highlights the need to communicate to different audiences, to both the medical profession and the end-user. Getting doctors to recommend the medicine and pulling the product through the channel by stimulating patient demand after a health scare are paramount.

**Originality/value** – This is the first pharmaceutical business case where the withdrawal of a rival product leaves the dominant competitor in a monopoly situation. Contrary to expectation, market share plummets despite the absence of competition.

**Keyword(s):**

Marketing communications; Marketing strategy; Pharmaceuticals industry; Drugs; Medical prescriptions.

His local pharmacy has become an important part of Jim's life in his later years. The 67 year old knows the routine all too well as he hands in his repeat prescription at the counter. The

friendly pharmacy assistants greet him by his name; they have come to know Jim well, he smiles at them and nod, “Another box of my usual, thanks”. Jim waits patiently for his pharmacist to fill his script, he rubs his protruding knuckles to try and ease the ever present pain. He no longer recognises his once strong hands; they have since been crippled and deformed by the relentless grip of his arthritis. The pharmacist knows of Jim's disabling condition and no longer asks him to sign for his prescription, but rather sign on his behalf to spare him his pride. Once his prescription is ready, Jim collects his medicine and exclaims, “Whatever did they do before Celebrex! I'll be back in a month to collect my next box; I can't go a day without them.”

**Arthritis**

Jim is not alone. Arthritis is a musculoskeletal disorder that is one of the most common causes of disability in the USA (Lawrence *et al.*, 1998). It is generally accepted that the occurrence of arthritis does not vary amongst people living in Europe or North America (Symmons *et al.*, 2002). Arthritis is often referred to as a single disease. It is a broad term for more than 100 medical conditions that affect the musculoskeletal system, more specifically joints (Yelin *et al.*, 2007). Arthritis is characterised by pain, stiffness, inflammation and damage to joints and can result in joint weakness, instability, deformities and bone fracture. The scope of the effects can range from chronic pain to disability that can interfere with even basic daily tasks, such as walking, writing and meal preparation (Yelin *et al.*, 2007). Of the 100 forms of arthritis, the most common type is osteoarthritis; with prevalence in the hands, knee and hip joints occurring frequently in European populations over the age of 50 years (Peterson, 1996). Some recent statistics have been released in a national costs study relating to arthritis and rheumatic conditions in the USA (Yelin *et al.*, 2007). Arthritis affects more than 46 million American adults (about one in five), osteoarthritis accounts for about 50 per cent of cases. As the population ages, the number of people with arthritis is expected to increase significantly. Current trends suggest that by 2030, 67 million US adults will suffer from some form of arthritis. Arthritis is not limited to the elderly; nearly two-thirds of arthritis sufferers are under the age of 65. Peterson (1996) report occurrence of the disease among a range of age brackets starting from as young as 25 years of age; the 45-54 and 55-64 categories in European populations. Among adults of working age (18-64 years) work limitations attributable to arthritis affect about one-third of those with arthritis. Overall, 19 million adults reported activity limitations due to arthritis. In 2003, the total cost of arthritis in the USA was $128 billion made up of both medical expenses and indirect costs, such as lost income (Yelin *et al.*, 2007). The burden of arthritis is not to be understated and involves both the economic costs as well as the impact on the individual's quality of life (Peterson, 1996).

**The pharmaceutical industry**

Medicines play a vital role in the treatment of arthritis. The pharmaceutical industry undertakes the development, production and supply of pharmaceutical products. The industry is under constant pressure to develop new, improved medicines that achieve superior health care. Not surprisingly, substantial Research and Development budgets are a distinguishing feature of the pharmaceutical industry. In the USA, pharmaceutical companies invested a combined $55.2 billion in Research and Development in 2006. The average cost of discovering and developing a new medicine is more than $1 billion, with development time spanning up to 15 years. Of the compounds discovered, only five of every 10,000 investigated reach the clinical trial stage of development. Of those five, only one is ever

approved for patient use. Once a pharmaceutical company has managed to get a new medicine to market, it still faces the challenge of recouping the cost of its development. On average only three out of ten medicines will recoup the cost of their development, clinical trials, registration and marketing. During the 1990s, the pharmaceutical industry witnessed the emergence of several blockbuster drugs each generating $1 billion in sales annually. The search for blockbuster discoveries was the strategy adopted by many of the big pharmaceutical companies as they recognised they could achieve shorter payback times. Other defining features of the pharmaceutical industry are the strict regulations governing the approval of new medicines and the tough controls over the promotion of pharmaceutical products. Despite such regulations, the pharmaceutical industry remains as one of the most successful and influential. Two key players in the global pharmaceutical industry include US-based companies, Pfizer Limited and Merck & Company.

**Direct-to-consumer advertising of prescription drugs**

Direct-to-consumer advertising (DTCA) of prescription drugs is strictly regulated in both the USA and in New Zealand, but the practice of using classic marketing communications tools is legal (Hoek and Gendal, 2004). The advertising of prescription drugs targeted directly to the public is a prohibited practice in most countries of the world, including Canada (Gardner *et al.*, 2003). With healthcare mainly funded privately by consumers in the USA, consumers tend to argue that learning about new drugs on the market should not be the exclusive domain of doctor to patient communications (Morris and Griffen, 1992). In the past, medical advertising was confined to scholarly medical journals read by doctors (Smith, 2006). This time lag between approval of a new drug and the doctor's knowledge was seen as inefficient, a process that could be improved upon by using DTCA. DTCA of prescription drugs in the USA mainly consists of promotional print materials in mass media (Barrett, 1998). The purpose of DTCA is to influence consumers to request prescriptions from their doctors (Hollon, 1999). Gardner (2003) lists three types of DTCA aimed at the general public:

1. product claim advertisements that promote the product name and therapeutic characteristics;
2. reminder type advertisements that keep the brand name current with consumers; and
3. help-seeking advertisements that inform customers about new treatments for diseases.

The net benefit to the pharmaceutical industry in the USA and New Zealand has been to increase demand for many of its products, with little impact on patient-doctor communications (Hoek and Gendall, 2004).

The purpose of this case study is to demonstrate how DTCA of prescription medicines can restore faith in the cyclooxygenase-2 (COX-2) (inflammation treatment) product category. Celebrex became the first of a new class of drugs known as selective non-steroidal anti-inflammatory drugs (NSAID's) for the treatment of arthritis. After the Federal Drug Administration required a “black box” warning due to CV health safety concerns, it became a strategic marketing exercise to communicate the benefits of this new drug to the mass consumer market, despite health safety concerns. This case study communicates the importance of exposing consumers experiencing daily pain to consider the facts using information in addition to the traditional doctor-patient consultation. It has implications for European countries and others such as Canada facing increasing pressure to consider DTCA legislation.

## Pfizer Limited

Pfizer Limited is the world's largest pharmaceutical company. Founded in 1849, Pfizer has its corporate headquarters in New York and its operations extend over 150 countries. Pfizer the research-based biomedical and pharmaceutical company works “to discover, develop, manufacture and deliver quality, safe and effective prescription medicines” (www.pfizer.com). Although Pfizer's (2008) pharmaceutical business accounts for the majority of its revenues, the company is also a successful competitor in the consumer health and animal health sectors. The 1990s was a period of significant growth and advancement for Pfizer pharmaceuticals and among its many success stories were a series of blockbuster drugs. Of particular fame are Lipitor (a cholesterol lowering drug), Zoloft (an antidepressant) and Viagra (used to treat impotence). Pfizer develops and distributes medicines to treat a broad range of medical conditions spanning the entire body.

## Merck & Company

Merck & Company is among the top seven largest pharmaceutical companies worldwide. Merck was first established in New York in 1891 and today has its headquarters in Whitehouse Station, New Jersey. The global research-driven pharmaceutical company operates in many countries under the name Merck Sharp & Dohme (2008). Merck discovers, develops, manufactures and markets vaccines and medicines that meet a diverse range of medical needs. Merck has experienced its own blockbuster success with a number of its prescription medications, including Zocor (a cholesterol lowering drug), Fosamax (an osteoporosis treatment) and Singulair (an asthma medicine), (www.msd.com).

## Traditional arthritis treatment

To date, there is no cure for arthritis and treatment consists of symptom management particularly pain relief. Most arthritis sufferers take pain medication daily to control their symptoms, improve function and ultimately increase their quality of life. Inflammation is the defining feature of arthritis and effective pain relief involves treating this inflammation. Anti-inflammatory drugs target the inflammation processes involved in arthritis. Until 1999, traditional NSAIDs were the treatment option of choice for arthritic patients. NSAIDs work by inhibiting the enzyme COX which produces prostaglandins within the body's cells. Prostaglandins promote inflammation and pain, they also protect the lining of the stomach. Within the body there are two forms of COX; COX-1 (produces prostaglandins that protect the stomach) and COX-2 (produces prostaglandins involved in inflammation). Traditional NSAIDs are non-selective, that is they act by blocking both COX-1 and COX-2 production. As a result they effectively treat inflammation, but can cause the unwanted side effects of stomach upset and ulcers. The gastric side effects are a cause for great concern given that they account for 20 per cent of all reported adverse drug events in the USA. Up to 40 per cent of NSAID users report gastric symptoms and about one in three long-term NSAID users will develop a stomach ulcer (Hassan-Alin *et al.*, 2005). These can result in serious consequences including hospitalisation and even death. In the USA, it has been estimated that there are over 100,000 hospital admissions per year and 16,500 deaths per year due to NSAID-induced gastric complications (Hassan-Alin *et al.*, 2005). There are many different traditional or non-selective NSAIDs available on the US market, both over-the-counter (OTC) and prescription only, including Ibuprofen (Advil®), Diclofenac (Voltaren®), Naproxen (Naprosyn®), Indomethacin (Indocin®), Ketoprofen (Orudis®) and Piroxicam (Feldene®). Refer to Table I for retail prices.

## COX-2 selective NSAID's

In the late 1990s, a drug entered the market that revolutionised the treatment of inflammation. Celebrex® became the first of a new class of drugs known as COX-2 selective NSAIDs. Celebrex offered a huge advantage over traditional NSAIDs by way of effectively treating inflammation, without compromising the protective lining of the stomach. It was the answer that the medical profession and patients had been waiting for, a drug that tipped the benefit/risk scales in the favour of the patient and would successfully achieve improved treatment for arthritis sufferers. Like most drug launches, Celebrex's entry to the market was a long time in the making. At the heart of its discovery was Philip Needleman, the scientist that first hypothesised that there were two kinds of COX enzyme. Dr Needleman shepherded celecoxib (the active ingredient in Celebrex) through the drug development pipeline. From 1989 Dr Needleman was the senior vice president and chief scientist of Monsanto Company and in 1993 he became president of Searle1Research and Development. He headed the team of medicinal chemists that researched and discovered the compound celecoxib which blocked COX-2, but spared COX-1. On 31 December 1998 the US Food and Drug Administration (FDA) approved Celebrex, the first selective COX-2 to gain approval.

## The Celebrex Launch

By early 1999, Celebrex was market ready and Searle established a USA co-promotional agreement with Pfizer, the world's largest pharmaceutical company. Searle had much to gain from joining forces with this pharmaceutical giant. Pfizer/Searle knew the superiority of their new, improved NSAID and the added value was captured in its price. Following extensive research of consumers, physicians, managed care organisations and computer modelling of competitors, the average wholesale price was set at $2.42 a capsule, ten to 20 times that of traditional NSAIDs (Spiegel and Gralnek, 2004). The Pfizer/Searle campaign targeted medical practitioners through a sales team of over 4,000 representatives involved in raising awareness among the medical profession and detailing doctors of the benefits of Celebrex. Accompanying the information was an abundant supply of Celebrex sample packs for doctors to use at their discretion. Study results and advertisements for Celebrex were placed in numerous medical publications to further capture the attention of doctors. To raise consumer awareness, Pfizer/Searle enlisted members of the American Gastroenterologist Association and sponsored a campaign that encouraged people with arthritis to take a quiz to establish if they were at risk of developing stomach ulcers, those found to be at risk were urged to talk to their doctor. After much anticipation Celebrex became widely available in February 1999 and the launch was the most successful in industry history. In its first year on the market, Celebrex sales exceeded $1.5 billion globally (*Monsanto Annual Report*, 1999). In 1999, there were 16.6 million total prescriptions filled for Celebrex, including 9.7 million new prescriptions written and 6.9 million refills (*Monsanto Annual Report*, 1999). The sales of Celebrex was driven by a powerful promotional campaign that continued to target both doctors and consumers.

## Enter Vioxx

Many pharmaceutical companies were aware of the new COX-2 selective class of drugs and were eager to enter this unique market. Merck & Company, another global research-driven pharmaceutical giant, had developed its own selective COX-2 inhibitor, rofecoxib, which they branded Vioxx®. Merck was working hard to propel Vioxx through the regulatory processes and gain FDA approval. This enabled Merck to launch Vioxx just months after

Celebrex. In May 1999, Vioxx entered the market; Celebrex was no longer the only drug in its class. Within days of approval, Merck's sales representatives, including members of a specialty sales force, fanned out to educate doctors about Vioxx and provide them with samples. Vioxx was priced comparably with Celebrex, with a similar premium over the price of traditional NSAIDs. Therapeutically and economically, there was no significant difference between Vioxx and Celebrex. In an effort to gain a competitive advantage both products were backed by impressive advertising budgets. In 2000, Merck spent over $160 million on DTCA and almost $80 million was spent to promote Celebrex (Porter, 2002). These are impressive marketing communications expenditures when one consider that in the same year $125 million was spent on Pepsi Cola, one of the most advertised soft drinks (Stanford University Medical Centre, 2005). The advertising campaigns paid off with Celebrex and Vioxx capturing one-third of the 111 million NSAID prescriptions for the year ending August 2000. Despite Merck's advertising expenditure on Vioxx being double that spent on Celebrex, Celebrex retained its position as COX-2 market leader.

**2000-2004**

Celebrex continued to narrowly outperform Vioxx. The advertising campaigns achieved widespread brand recognition and people with pain from causes other than arthritis began to ask their doctors about the “newer, better anti-inflammatories”. This in effect expanded the COX-2 market by eroding the traditional NSAID market and increasing the total demand for painkillers. In 2002, the makers of Celebrex released a second Cox-2 inhibitor, valdecoxib, under the brand name Bextra®. Once again Pfizer agreed to be a co-promotional partner. Through a series of acquisitions, Pfizer gained complete control of both Celebrex and Bextra in 2003. Over the subsequent years, Pfizer and Merck both enjoyed the benefits associated with the healthy growth of the COX-2 market. The companies continued to investigate other possible uses for their COX-2 inhibitors in an effort to gain FDA approval for additional indications.

**Vioxx withdrawal**

On 30 September 2004 Merck announced the voluntary, worldwide withdrawal of Vioxx (refer to Appendix 1). The landmark decision came following evidence that Vioxx increased the risk of serious CV events, including heart attacks and stroke. The findings were revealed in the Adenomatous Polyp Prevention on Vioxx (APPROVe) study, which was designed by Merck to broaden the medical conditions that Vioxx was indicated to treat. The APPROVe clinical trial was also designed to further assess the CV safety of Vioxx and refute ongoing criticism. As early as mid-2000, concerns had been raised over the effects of Vioxx on the heart. In June 2000, the FDA received results from Merck's Vioxx Gastrointestinal Outcomes Research (VIGOR) study that found an increased risk of serious CV events in patients taking Vioxx compared to patients taking naproxen (a traditional NSAID) (*FDA News*, 2004). The FDA took considerable time deliberating over the VIGOR results along with other available data, consulting with its Arthritis Advisory Committee regarding the interpretation of the safety information. The FDA took until April 2002 to formulate its response to the VIGOR findings, which involved strict labelling requirements for Vioxx. The labelling changes included warnings about the increase in risk of CV events, including heart attack and stroke. Merck obeyed the new labelling conditions and continued to promote the effectiveness and safety of Vioxx. The warnings did not seem to have a significant impact on sales, with 2003 Vioxx global sales totalling $2.5 billion.

Evidence was mounting regarding Vioxx's CV safety and the APPROVe results could not be ignored. Of great concern was the number of people taking Vioxx. Since its launch in May 1999 to August 2004 it was estimated that there were 105 million prescriptions written for Vioxx in the USA alone, representing approximately 20 million American patients (www.merck.com). The APPROVe results called for immediate action to be taken and Merck opted for a proactive strategy involving withdrawing Vioxx on its own terms as opposed to defending Vioxx against inevitable scrutiny and backlash. Raymond Gilmartin, chairman, president and chief executive officer of Merck commented on the decision:

Although we believe it would have been possible to continue to market Vioxx with labelling that would incorporate these new data, given the availability of alternative therapies and the questions raised by the data, we concluded that a voluntary withdrawal is the responsible course to take (Barclay, 2004).

There was no denying that Vioxx was a blockbuster drug for Merck and a vital contributor to the company's revenue. Merck knew that it would suffer greatly from the Vioxx withdrawal. However, Merck was very calculating in its decision and in weighing up the options concluded that withdrawal was most appropriate course of action. No doubt minimising the risk of medical liability was a key motive. The enormity of Merck's decision to remove Vioxx from the market was reflected in news of the withdrawal flooding the global media.

**Impact on Merck**

As anticipated the Vioxx withdrawal hit Merck hard. The financial burden associated with the 2004 withdrawal had an immediate effect on Merck's results. In 2004, Merck observed an estimated $1.24 billion reduction in sales; consisting of $490 million due to customer returns of Vioxx and up to $750 million in forgone sales of Vioxx for the fourth quarter. Not only were sales down, but also expenses were up including $141.4 million of expenditure to undertake the withdrawal of Vioxx and $93.2 million related to write-offs of Vioxx stock held by Merck. Additionally, the company set aside a reserve of $675 million solely for its future legal defence costs related to Vioxx litigation, this did not allow for any potential liability as a consequence of such litigation. As of 31 January 2005 Merck had been served with approximately 850 lawsuits, which included over 2,400 plaintiff groups alleging personal injuries as a result of taking Vioxx. Further lawsuits had been filed against Merck by various shareholders of the company, accusing Merck of making false and misleading statements regarding Vioxx. The legal struggle was not contained to the USA with lawsuits also filed in Europe, Australia, Canada, Brazil and Israel. Merck's annual report, 2004 reflects on the unfavourable consequences of the Vioxx withdrawal (www.merck.com).

**A doubtful market**

Merck's exit from the COX-2 market in 2004 left Pfizer as the only remaining team with its two key players, Celebrex and Bextra. Under other circumstances this competitive free atmosphere would appear as the ideal market. However, the Vioxx withdrawal had left it a doubtful market for there was uncertainty as to whether or not the CV risks associated with Vioxx extended across the entire COX-2 class of drugs. The Vioxx controversy placed the spotlight on the COX-2 inhibitor class and both Celebrex and Bextra were subjected to immense scrutiny. The FDA was on alert and determined to avoid further embarrassment and criticism. The safety of Celebrex had been called into question as early as December 2004, just months after the withdrawal of Vioxx. The Adenoma Prevention with Celebrex study

conducted by the National Cancer Institute findings revealed an increased risk of heart problems with patients taking Celebrex. On 17 December 2004 the FDA ordered Pfizer to suspend all DTCA of Celebrex while the agency evaluated the available information regarding the safety of Celebrex. During the period Pfizer was permitted to continue selling Celebrex.

**Implications for Pfizer**

The FDA undertook lengthy proceedings and thorough analysis of the available evidence for all NSAIDs. From 16 February 2005, a three-day, intensive meeting of the Drug Safety and Risk Management Advisory Committee and the Arthritis Advisory Committee was held to discuss the risks and benefits of the NSAID class of drugs. The main objective of the meeting was to decide on an appropriate course of action and make recommendations to the FDA. The committees struggled to reach agreement on the fate of individual drugs, recognising the need for further studies into the safety of NSAIDs. It took a further couple of months until the FDA announced its stance (refer to Appendix 2). In April 2005, the FDA called for the withdrawal of Bextra, after it concluded that the risks outweighed the benefits. Pfizer cooperated with the FDA and Bextra was removed from the market on 7 April 2005. Although Bextra was not as lucrative a product as Celebrex, it was still a strong seller and withdrawal was a blow to Pfizer wiping out $1.3 billion annual sales. At the same time, the FDA called for Pfizer to place a “black box”, the most serious type of warning, on the Celebrex label. The boxed warning was to highlight the potential for increased risk of heart attacks and stroke and stomach bleeding associated with Celebrex use. It would appear that Celebrex was not singled out, as manufactures of all prescription NSAIDs were required to revise their labelling to include the same boxed warning as Celebrex. Dr Joseph Feczko, Pfizer's chief medical officer commented on the new labelling requirements:

We have worked closely with the FDA to ensure that Celebrex's label provides physicians and patients with the information they need to make the most appropriate and most informed treatment decisions (www.consumeraffairs.com).

The “black box” warning was the FDA's last resort before issuing notification of recall. Celebrex had narrowly escaped having to be withdrawn, much to relief of Pfizer. In the eyes of Pfizer keeping Celebrex on the market was of upmost importance. Celebrex remained the only COX-2 inhibitor available to the millions of arthritis and pain sufferers. Celebrex now had a monopoly, but the COX-2 market was not the prospering multi-billion dollar market it once was. Doctors and patients viewed COX-2 inhibitors with great caution and prescription numbers plummeted. Certainly following the withdrawal of Vioxx in December 2004, Pfizer would have hoped to capture Vioxx's $2.5 billion share of the market in 2005. However, Pfizer's inability to capture the additional market share was reflected in the decline in Celebrex sales from 2004 to 2005 (Figure 1). Ongoing safety concerns of all COX-2 inhibitors coupled with the lack of Celebrex advertising would have no doubt contributed to the dramatic reduction in Celebrex sales. Indeed, Celebrex had not emerged from the Vioxx scandal unscathed.

**Pharmaceutical promotion tools – restoring the faith**

Medical doctors have a special role in the consumer decision-making process of pharmaceutical products. In most countries of the world consumers have little influence or no choice of the drug or brand; the decision is made by the medical practitioner (Pitt and Nel,

1988). Marketing of prescription drugs is to and through the medical profession (Smith, 2006; Pitt and Nel, 1988). In a study measuring the relative influence of advertising to influence prescribing behaviour by doctors, Pitt and Nel (1988) found that personal experience with the product was the most influential factor. The implications are that Pfizer could use the influence of the doctor to restore the public's confidence in Celebrex. In the USA, they had an additional tool to broaden the reach of the advertising message. The USA and New Zealand markets allowed DTCA. The company decided to focus its efforts on addressing the concerns of both the medical profession and patients regarding the safety of Celebrex. In response to their concerns and questions, Pfizer communicated the risks and benefits of Celebrex. In October 2006, Pfizer commenced the prospective randomized evaluation of Celecoxib integrated safety versus ibuprofen or Naproxen study, to further understand the safety of Celebrex in comparison to traditional NSAIDs. In April 2006, Pfizer reintroduced Celebrex direct-to-customer advertising in the USA. The new advertisements were vastly different to those used in the past. Rather than merely emphasising the ability of Celebrex to effectively ease arthritis pain, the new campaign took care to directly talk about the side effects of Celebrex and stress that Celebrex still represented a good treatment option for some patients. The unconventional, two-and-a-half minute advertisement was used as an opportunity to educate patients about Celebrex. The animated television commercial was made up of only white lines on a blue background; on closer inspection of the lines it is revealed that they are the words from the package inserts of Celebrex and other drugs. These lines are used to create graphics of people running, dancing and cycling (refer to Figure 2). The advertisement does not shy away from the boxed warning pertaining to Celebrex, but rather emphasises that all NSAIDs are required to carry the same boxed warning. Also mentioned in the advertisement is the fact Celebrex has never been taken off the market and the importance of treatment options for patients. The promotion cleverly conveys the message and encourages patients to talk to their doctors about Celebrex. By September 2006, the number of new prescriptions for Celebrex had risen by 9 per cent. Doctors were once again recommending the medicine and there was renewed demand by patients wanting to take Celebrex to relieve their pain.

**Controlling pain versus healthy hearts**

Presently, Celebrex maintains its monopoly of the COX-2 inhibitor market. The damaged reputation of the COX-2 class has discouraged new entrants and has made the medical profession and patients cautious. Pharmaceutical companies realise that need to recover lost ground in the COX-2 market to return to former glory. In matters concerning public health, safety concerns resonate long after the product withdrawal from the market. The devastating blow was felt not only by Merck, but by all stakeholders including patients, the medical profession, the FDA, NSAID market and even Merck's rival Pfizer also. The Vioxx withdrawal impacted the entire NSAID market suggesting the CV risks were class effects and not isolated to Vioxx. The aftermath of the “Vioxx withdrawal” endures years after its occurrence; however, as they say “time heals all wounds”. And whilst it is too early to determine whether the COX-2 market will ever fully recover from Vioxx, one fact remains, patients still have a strong need for pain relief.

There is one constant throughout all this and that is the patient. Over the past few years of drug withdrawals and labelling changes, patients have continued to seek treatment for their pain. There are many people in the same situation as Jim that dread to think how they would cope without Celebrex. Celebrex has been proven effective for millions of arthritis sufferers worldwide and has achieved relief for those who previously believed their pain was

untreatable. Arthritis and other conditions involving pain are unlike many medical conditions where patients do not experience any symptoms. There are varying degrees of pain, but its presence is difficult to ignore. For medical conditions that have numerous signs and symptoms, it is often the symptom of pain that motivates the patient to seek help. New research goes even further suggesting that pain causes arthritis (Fiorentino *et al.*, 2008). Many pain sufferers rely on pain relievers to get them out of bed of a morning and help them through their day. To deny patients of effective pain options is to rob them of their quality of life. With this in mind Pfizer stands behind Celebrex and is committed to ensuring its availability to patients, particularly those suffering from arthritis.

**Managerial implications for the Celebrex brand**

The Vioxx withdrawal had resulted in public health safety concerns for regulators, the medical profession and the public at large. It highlighted the risks of using a similar product such as Celebrex after the CV health warnings related to the COX-2 market. Management will need to make an assessment of how to approach future marketing campaigns for a product with a "black box" label as required by regulators. Celebrex is not unique in marketing risky pharmaceutical products; for example, a similar risky situation exists with selective serotonin reuptake inhibitors antidepressants.

The continued use of DTCA remains a persuasive tool to win back targeted consumers such as chronic pain sufferers. Different age categories and the different types of musculoskeletal diseases are good bases for developing market segmentation strategies. Each segment can be successfully targeted with DTCA. The challenge to management would be to define the segmentation variables that could assist the Celebrex brand to overcome a known public health safety scare. One variable for segmenting markets suitable for use of COX-2 products is an assessment of evidence of risk to CV disease (Wong *et al.*, 2005). One of the recommendations of this study is to:

[…] adapt from a strategy of "blockbuster overreach" to a more segmented market indication, perhaps coupled with the use of biomarkers to detect existing or emerging risk of drug related adverse effects (Wong *et al.*, 2005).

An opportunity exists for Celebrex management to combine the predictive ability of medical science research and existing marketing segmentation skills to benefit consumers less prone to CV disease.

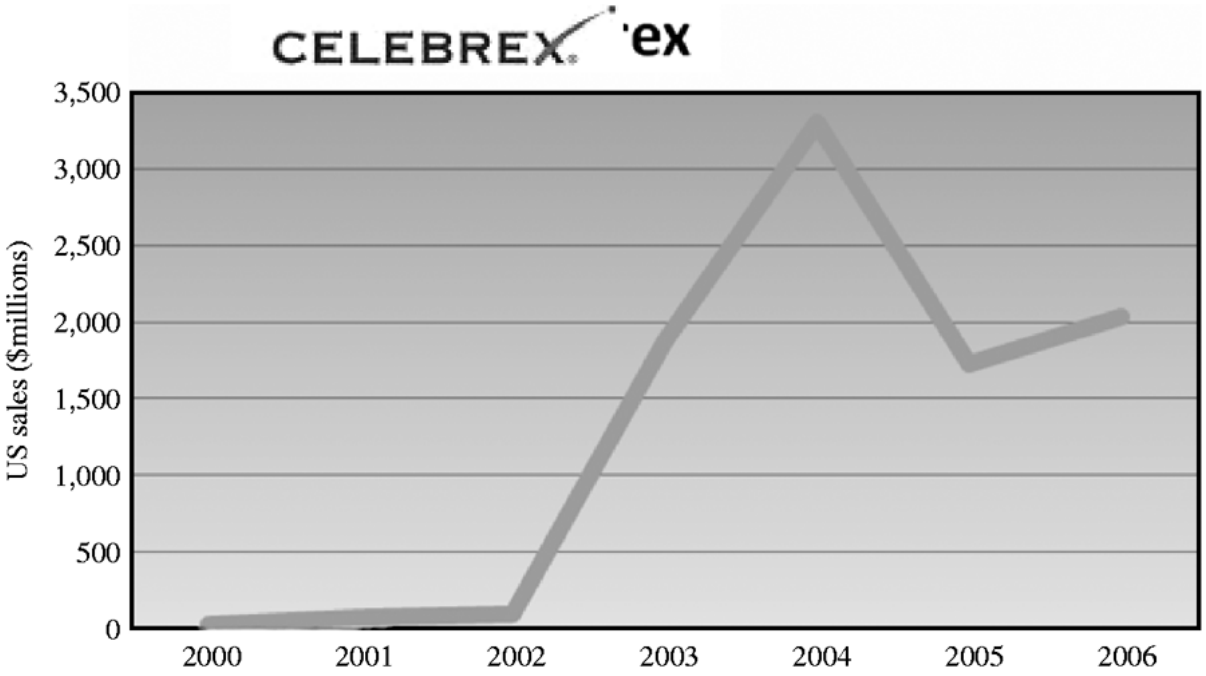
A second challenge for Celebrex management is the question how to build the brand in markets that prohibit the use of DTCA. Currently, this challenge applies to most countries in the world except the USA and New Zealand (Gardner *et al.*, 2003). Innovative brand managers have been complying with the letter of the law by using "un-named product" print advertising targeting customers in Australia. An example is the Viagra "Welcome back Tiger" campaign directed at consumers without the product brand name (Hall and Jones, 2006). The Viagra advertisement feature a mature male with a tiger head sitting next to a satisfied looking female. A specific example of brand building using "un-named product" advertisements was the Arthritis Foundation advertisement telling arthritis patients to ask their doctors about a new drug. The advertisement acknowledged a sizable cash donation by the manufacturers of Celebrex (Barry, 2000). Australia is regulated by similar regulation as found in European markets with few complaints targeting consumers using the un-named product advertising strategies (Hall and Jones, 2006). There is evidence to suggest that

countries in the Northern hemisphere with sophisticated health care infrastructure will experience an increasing trend towards DTCA as health care marketing and branding is tested in mass media applications (Langreth and Herper, 2006).

Finally, when the Celebrex patent expires, generic competitors will force management to compete with an equal drug that is substantially less expensive to the customer. Is there room for a re-evaluation of their pricing policy? Pfizer is enjoying sole supplier status after the withdrawal of Vioxx. A lower price presents an opportunity to grow the market while there is little or no competition. It might just be their best strategy going forward judging by the statements of a new President Obama who has indicated to fight big pharmaceuticals to lower drug costs. Some even argue that DTCA is facing increasing opposition, in an effort to make health care more affordable in the USA (Gregory, 2009). There is no doubt Pfizer has much to ponder and forward strategic marketing planning is paramount.

MERCK

*Fixed graphic 1*




**Source:** Sales figures sourced from Pfizer Annual Reports 2000-2006

***Figure 1***

***Figure 2***

| Product | Amount (mg) | Quantity of tablets | Retail price (US$) |
|---|---|---|---|
| Advil | 200 | 200 | 14.99 |
| Voltaren | 25 | 60 | 58.09 |
| Naprosyn | 500 | 30 | 59.99 |
| Indomethacin | 25 | 30 | 14.99 |
| Ketoprofen | 75 | 60 | 14.99 |
| Piroxicam | 20 | 30 | 14.99 |
| CELEBREX | | 30 | 120.91 |

**Source:** Retail prices sourced from: www.drugstore.com (22 March 2008)

**Table I.**

***Table I***

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**Further Reading**

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**Appendix 1. Merck announces voluntary worldwide withdrawal of Vioxx®**

Fixed graphic 1

Whitehouse Station, New Jersey, 30 September 2004 – Merck & Co., Inc. today announced a voluntary worldwide withdrawal of VIOXX® (rofecoxib), its arthritis and acute pain medication. The company's decision, which is effective immediately, is based on new, three-year data from a prospective, randomized, placebo-controlled clinical trial, the APPROVe trial.

The trial, which is being stopped, was designed to evaluate the efficacy of VIOXX 25 mg in preventing recurrence of colorectal polyps in patients with a history of colorectal adenomas. In this study, there was an increased relative risk for confirmed CV events, such as heart attack and stroke, beginning after 18 months of treatment in the patients taking VIOXX compared to those taking placebo. The results for the first 18 months of the APPROVe study did not show any increased risk of confirmed cardiovascular events on VIOXX, and in this respect, are similar to the results of two placebo-controlled studies described in the current US labelling for VIOXX.

“We are taking this action because we believe it best serves the interests of patients,” said Raymond V. Gilmartin, chairman, president and chief executive officer of Merck. “Although we believe it would have been possible to continue to market VIOXX with labelling that would incorporate these new data, given the availability of alternative therapies and the questions raised by the data, we concluded that a voluntary withdrawal is the responsible course to take.”

APPROVe was a multi-center, randomized, placebo-controlled, double-blind study to determine the effect of 156 weeks (three years) of treatment with VIOXX on the recurrence of neoplastic polyps of the large bowel in patients with a history of colorectal adenoma. The trial enrolled 2,600 patients and compared VIOXX 25 mg to placebo. The trial began enrollment in 2000.

**VIOXX® (rofecoxib) is a registered trademark of Merck & Co., Inc.**

VIOXX was launched in the USA in 1999 and has been marketed in more than 80 countries. In some countries, the product is marketed under the trademark CEOXX. Worldwide sales of VIOXX in 2003 were $2.5 billion.

Results of the VIGOR study, released in March 2000, demonstrated that the risk of gastrointestinal (GI) toxicity with VIOXX was less than with naproxen, but indicated an increased risk of CV events versus naproxen. However, in other studies including Merck's Phase III studies that were the basis of regulatory approval of the product, there was not an increased risk of CV events with VIOXX compared with placebo or VIOXX compared with other non-naproxen NSAIDs. Merck began long-term randomized clinical trials to provide an even more comprehensive picture of the CV safety profile of VIOXX.

“Merck has always believed that prospective, randomized, controlled clinical trials are the best way to evaluate the safety of medicines. APPROVe is precisely this type of study – and it has provided us with new data on the CV profile of VIOXX,” said Peter S. Kim, PhD, president of Merck Research Laboratories. “While the cause of these results is uncertain at this time, they suggest an increased risk of confirmed CV events beginning after 18 months of continuous therapy. While we recognize that VIOXX benefited many patients, we believe this action is appropriate.”

Merck has informed the US FDA and regulatory authorities in other countries of its decision. The company also is in the process of notifying health care practitioners in the USA and other countries where VIOXX is marketed. Patients who are currently taking VIOXX should contact their health care providers to discuss discontinuing use of VIOXX and possible alternative treatments. In addition, patients and health care professionals may obtain information from www.merck.com and www.vioxx.com, or may call (888) 36-VIOXX (1-888-368-4699).

The results of clinical studies with one molecule in a given class are not necessarily applicable to others in the class. Therefore, the clinical significance of the APPROVe trial, if any, for the long-term use of other drugs in this class, consisting of COX-2 specific inhibitors and NSAIDs, is unknown. The company will work with regulatory authorities in the 47 countries where ARCOXIA is approved to assess whether changes to the prescribing information for this class of drugs, including ARCOXIA, are warranted. Merck is continuing to seek approval for ARCOXIA in other countries, including the USA.

Merck will continue its extensive clinical program to collect additional longer-term data for ARCOXIA, its medication for arthritis and acute pain.

With regard to financial guidance, prior to today's announcement, Merck remained comfortable with its 2004 earnings per share guidance of $3.11-$3.17. The company currently expects earnings per share to be negatively affected by $0.50-$0.60 as a result of today's announcement. This estimate includes forgone sales, write-offs of inventory held by Merck, customer returns of product previously sold and costs to undertake the pullback of the product. Included in this cost estimate is the expectation of forgone fourth quarter sales of VIOXX of $700-$750 million. In addition, Merck expects that worldwide approximately one month of inventory is held by customers and will be returned.

At this point, it is uncertain which of these costs will be recorded in the third quarter and which will be recorded in the fourth quarter. Therefore, at this point, Merck is retracting the third quarter guidance it had previously provided.

Merck will report third-quarter earnings on October 21. At that point, the company will provide additional information regarding the costs for product withdrawal.

**About Merck**

Merck & Co., Inc. is a global research-driven pharmaceutical company. Merck discovers, develops, manufactures and markets a broad range of innovative products to improve human and animal health, directly and thorough its joint ventures.

**Forward looking statement**

This press release contains “forward-looking statements” as that term is defined in the Private Securities Litigation Reform Act of 1995. These statements involve risks and uncertainties, which may cause results to differ materially from those set forth in the statements. The forward-looking statements may include statements regarding product development, product potential or financial performance. No forward-looking statement can be guaranteed, and actual results may differ materially from those projected. Merck undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events, or otherwise. Forward-looking statements in this press release should be evaluated together with the many uncertainties that affect Merck's business, particularly those mentioned in the cautionary statements in item one of Merck's Form 10-K for the year ended 31 December 2003 and in its periodic reports on Form 10-Q and Form 8-K (if any), which the company incorporates by reference.

**Appendix 2. FDA news**

For Immediate Release Media Inquiries: Kathleen Quinn

P05-16 301-827-6242

7 April 2005 Consumer Inquiries: 888-INFO-FDA

The FDA today announced a series of important changes pertaining to the marketing of the non-steroidal anti-inflammatory class of drugs, including COX-2 selective and prescription and non-prescription (OTC) non-selective NSAID medications. A list of these products is available on the internet at: www.fda.gov/cder/drug/infopage/cox2/default.htm

“Today's actions protect and advance the health of the millions of Americans who rely on these drugs everyday,” said Dr Steven K. Galson, Acting Director of FDA's Center for Drug Evaluation and Research. “FDA is providing the public information based on the latest available scientific data to guide the careful and appropriate use of these drugs aimed at maximizing their potential benefits and minimizing their risks.”

FDA has asked Pfizer, Inc. to withdraw Bextra (valdecoxib) from the market because the overall risk versus benefit profile for the drug is unfavorable. FDA has also asked Pfizer to include a boxed warning in the Celebrex (celecoxib) label. Pfizer has agreed to suspend sales

and marketing of Bextra in the USA, pending further discussions with the agency. Pfizer has agreed to work with FDA on the boxed warning for Celebrex. FDA is asking manufacturers of all other prescription NSAIDs to revise their labels to include the same boxed warning highlighting the potential for increased risk of CV events and GI bleeding associated with their use. Manufacturers of Celebrex and all other prescription NSAIDs will be asked to revise their labelling to include a medication guide for patients to help make them aware of the potential for CV and GI adverse events associated with the use of this class of drugs.

In addition, FDA is asking the manufacturers of all OTC NSAIDs to revise their labels to include more specific information about the potential CV and GI risks, and information to assist consumers in the safe use of the drugs. FDA is also asking manufacturers of OTC NSAIDs to include a warning about potential skin reactions. The labelling of the prescription NSAIDs already addresses potential skin reactions.

This current reexamination of the CV risks of NSAIDs began after Merck conducted a voluntary worldwide withdrawal of its COX-2 selective NSAID, Vioxx (rofecoxib), in September 2004. FDA will carefully review any proposal from Merck for resumption of marketing of Vioxx.

These actions are based on the available scientific data, including data accumulated since the drugs were approved. The FDA has carefully considered the presentations, discussions and recommendations from the joint meeting of the Agency's Arthritis and Drug Safety and Risk Management Advisory Committee held on 16-18 February 2005.

To inform the public and healthcare community of its decisions, FDA today issued a public health advisory and updated patient and healthcare practitioner fact sheets.

**About the authors**

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