

# CHAPTER I

## INTRODUCTION

This Chapter comprised three parts including rationale, objectives and expected benefit. The detail was described in the following:

### **Rationale and Statement of the Problem**

Specific Cyclo-oxygenase II (COX II) Inhibitors, which are a new subclass of nonsteroidal anti-inflammatory drugs, have been introduced in several countries for the relief of chronic pain in rheumatoid arthritis and osteoarthritis. Celecoxib and rofecoxib are members of these specific COX II inhibitors. This specificity is a decreasing gastric side effect compared with earlier NSAIDs, but adverse reactions have been common. Specific COX II inhibitor is more expensive than the other kind of NSAIDs. Demand for specific COX II inhibitors will lead to substantial additional cost. In the United States, celebrex<sup>®</sup> was the 10<sup>th</sup> best-selling drug on the market in 2001. Vioxx<sup>®</sup> ranked 13<sup>th</sup>, with 23.7 million prescriptions filled. Celebrex<sup>®</sup> (jointly marketed by Pharmacia and Pfizer) generated worldwide sales of \$3.1 billion and the worldwide sales of vioxx<sup>®</sup> were \$2.6 billion (1).

In Thailand, there had been an increasing trend of specific COX II inhibitors utilization since 1999; celecoxib dramatically increased while rofecoxib slightly increased as shown in Table 1.1.

Table 1.1: Estimated Cost of specific COX II inhibitors Utilization in Thailand between 1999 to 2001.\*

Drug Name	1999	2000	2001
	Cost** (Million Baht)	Cost** (Million Baht)	Cost** (Million Baht)
Celecoxib 200 mg	45.1	77.8	295.6
Rofecoxib 12.5 mg	7.7	17.1	36.0
Rofecoxib 25 mg	12.4	38.9	119.8
Total Cost (Million Baht)	65.2	133.8	451.4

\* Data from Drug Control Division of Thai Food Drug and Administration.

\*\* Estimated Cost based on Lerdsin Hospital price list.

The high cost of specific COX II inhibitors and the particular benefit in those at high risk for gastrointestinal adverse events led the National Institute for Clinical Excellence (NICE) in the UK to make recommendations for the use of these agents. They proposed that specific COX II inhibitors were not recommended for routine use in patients with rheumatoid arthritis (RA) or osteoarthritis (OA). They should be used, in preference to standard NSAIDs, when clearly indicated as part of the management of RA or OA only in patients who may be high risk of developing serious gastrointestinal adverse effects. NICE also indicated that the cost-effectiveness of the specific COX II inhibitors would be more favorable in high risk group (2).

Several studies in the following; investigate economic impact of using specific COX II inhibitors and some employ specific intervention to improve drug use.

In the US, Medicaid health maintenance organization developed and implemented a prior authorization policy (PA policy) for the use of the newer, the higher price of specific COX II inhibitors. This policy used criteria for appropriate use of celecoxib. The study found that estimated cost saving over study period for 415 denied prescriptions (from total 1329 prescriptions) was \$300,000 per 5 months or nearly \$700,000 a full year (3).

Graudins and colleague (4) studied the pattern of usage of specific COX II Inhibitors in The Prince of Wales Hospital (POWH) over a seven-week period during

August to October 2000. They collected data prospectively for patients who received celecoxib. Medication charts and prescriptions for celecoxib presented to the hospital pharmacy for both inpatients and outpatients were reviewed by pharmacists using standard data collection form. Data collection included patient demographic features, details of prescriber, indication for celecoxib use, detail of previous NSAID use and any adverse effects with previous NSAID or celecoxib. Of the 70 patients available for review, 50% had been prescribed celecoxib by their general practitioner prior to an admission. All of these patients were prescribed celecoxib for rheumatoid arthritis, osteoarthritis or chronic pain conditions. Of the patients prescribed celecoxib by hospital prescribers, only eight (23%) were considered to have an appropriate indication, based on the hospital's Pharmacy and Therapeutics Committee (PTC) guidelines. The largest category of inappropriate use in hospital was for acute pain (40%). A substantial proportion of patients (43%) were prescribed celecoxib as first line rather than second line therapy. An inappropriate prescribing of specific COX II inhibitors has both clinical and economic consequences. It requires further evaluation and appropriate intervention to improving rational drug use.

In Canada, a study reported that treatment of patients with osteoarthritis aged  $\geq 65$  years, rofecoxib has a slightly higher acquisition cost than other commonly used NSAIDs (\$1.60 vs \$1.67 per patient per day, 2000 Canadian dollars): this leads to an incremental annual cost of \$24.45 per patient using rofecoxib (5).

In Thailand, a cross-sectional descriptive study related to NSAIDs and selective COX II inhibitors was performed at Rajavithi Hospital by Phochanukul (6). The data was collected during a 5 weeks period in the orthopedics outpatient clinic. Only paid prescriptions were selected including 1,042 (61.9%) reimbursement prescriptions and 642 (38.1%) non-reimbursement prescriptions. There were marked differences between reimbursement and non-reimbursement groups in amount, type, group of NSAIDs, and dispensing values. The ratio of Essential Drug (ED) to Non-Essential Drug (NED) used in the reimbursement and non-reimbursement groups was 1:6 and 1:2.6, respectively. In the reimbursement group, 53% of the drug expenditure came from using selective COX II inhibitors, nimesulide or nabumetone and only 5% of drug expenditure came from specific COX II inhibitor, celecoxib. However, in the non-reimbursement group 60% of the drug expenditure came from using classical NSAIDs and 17 % of drug

expenditure came from specific COX II inhibitor. There was a tendency to prescribe new generation NSAIDs more than the classical NSAIDs. The most frequent prescribing pattern was single used of NSAID. Average cost per prescription for reimbursement group was 532.89 baht and it was 230.05 baht for non-reimbursement group. However this research did not study drug cost waste in low risk patients who received specific Cox II inhibitors.

Another study focused on the use of celecoxib and rofecoxib in orthopedic outpatients of Lerdsin Hospital (7). The purpose of this study was to analyze problem of using celecoxib and rofecoxib in terms of effectiveness, safety, drug cost and compliance of patients. The subjects of this study were 150 orthopedic outpatients. Average age was  $55 \pm 1.0$  years. Data based on the interviewing questionnaire were collected during August 1, 2001 to November 30, 2001. The results showed that 32 % of patients had two co-morbidities including OA plus hypertension and RA plus peptic ulcer, 48.7% of patients had no symptom of GI adverse effect after receiving specific COX II inhibitors and 81.3% of patients had ever taken prior NSAIDs. Sixty-five percentages were Civil Servant Medical Benefit Scheme (CSMBS). Thirty percent of drug cost per visit was 601-900 Baht, 26% was greater than 1,500 Baht, 19% was 901-1,200 Baht, 13% was 1,201-1,500 Baht and 10% was 301-600 Baht.

Based on our review, the studies in Thailand did not focus on cost impact. No studies to date have conducted a cost analysis between specific COX II inhibitors versus classical NSAIDs in low risk group. Thailand has limited health care budget. Although, the patients who had health insurance plan or pay by out of pocket can afford this expensive drug, the efficient use of resources, should be considered. Concerning the cost impact from increasing use of specific COX II inhibitors, this study explored the used of this drug in real practice. The objectives of this study were to characterize the patterns of usage of specific COX II inhibitor, and to determine economic impact of using specific COX II inhibitor in patient who are in the low risk and high risk groups.

## **Objectives**

The objectives of this study are the following;

1. To characterize the patterns of use of specific COX II inhibitors in orthopedic outpatients at Lerdsin Hospital.
2. To determine cost impact of using specific COX II inhibitors in orthopedic outpatients who are in low risk and high risk gastrointestinal adverse effects.

## **Expected Benefit**

The benefit from this study are;

1. The result of this study will provide cost data of using specific COX II inhibitors in substitution of conventional NSAIDs.
2. The result can be used for reducing cost of inappropriate treatment of specific COX II inhibitors.
3. The result will stimulate Pharmaceutical and Therapeutic Committee to implement drug use evaluation for effective but highly expensive drugs.