# CHAPTER IV

# RESULTS

This chapter comprised eight parts including, number of studied prescriptions, patients' characteristics, pattern of drug use, duration of therapy, indications for use, high risk factors, high risk and low risk ratio and cost waste.

## Number of Studied Prescriptions

During November and December 2002 at Lerdsin Hospital, 4,471 prescriptions were prescribed by orthopedists. Of these, 1,242 prescriptions were for specific COX II inhibitors and 3,229 prescriptions were for other kinds of NSAIDs. Of the 1,242 specific COX II inhibitors prescriptions, 425 prescriptions were for celecoxib and 817 prescriptions were for rofecoxib. For celecoxib prescriptions, 202 were in November and 223 were in December. For rofecoxib prescriptions, 428 were in November and 389 in December. The proportionate sample prescriptions of celecoxib were 91 in November and 94 in December. The proportionate sample prescriptions of rofecoxib were 170 in November and 164 in December. The proportionate sample prescriptions of NSAIDs were 296 in November and 298 in December. The proportionate sample differed from planning. The detail of proportionate sample was described in Appendix B. Total celecoxib prescriptions were 185, rofecoxib prescriptions were 334 and NSAIDs prescriptions were 549. Figure 4.1 shows the number of specific COX II inhibitors prescriptions and NSAIDs prescriptions which were used for determining whether patients at high risk of NSAIDs use.

## Patients' Characteristics

All prescriptions were encountered in orthopedic outpatient clinic during the study time. The characteristics of orthopedic outpatients are given in Table 4.1.

Eighty percent of patients receiving specific COX II inhibitors were female, 66% of patients receiving NSAIDs were female.

Concerning age of patients, 35.1% of specific COX II inhibitors group and 15.3% of NSAIDs group were patients aged ≥ 65 years. Chi Square Test ($\chi^2$) could be used to test whether there was an association between age and patient receiving specific COX II inhibitors. From $\chi^2$ test, there was an association between age and patient receiving specific COX II inhibitors. The result showed that, number of patients aged ≥ 65 years receiving specific COX II inhibitors more than number of patients aged ≥ 65 years receiving NSAIDs ($P < 0.0001$).

Sixty two percent of specific COX II inhibitors of patient were married status, and 55.1% of NSAIDs of patient was married. Ninety seven percent of specific COX II inhibitors and 99.2% of NSAIDs were prescribed to Thai Nationality. Almost all of the patients in both groups were Buddhist.

Concerning the occupation, 27.0% of specific COX II inhibitors group was housewives or work at home, followed by civil servant (15.8%). In contrast, 24.1% of NSAIDs was general employee, followed by housewives or work at home (18.2%).

Over 50% of patients for specific COX II inhibitor use and NSAIDs use paid for their medications themselves. Twenty nine percent of patients receiving specific COX II inhibitor were Civil Servant Medical Benefit Scheme (CSMBS) while 12% of patients receiving NSAIDs were CSMBS. Only 2% of patients receiving specific COX II inhibitors were Social Security Scheme (SSS) while 15% of patients receiving NSAIDs were SSS. Only 1% of patients receiving specific COX II inhibitors were universal coverage payment status while 6.7% of patients receiving NSAIDs were UC.

Based on our observation, it appeared that the number of patient in CSMBS group received specific COX II inhibitors was greater than the number of patient who received NSAIDs. We conducted Chi Square test ($\chi^2$) whether there was an association between CSMBS and patients receiving specific COX II inhibitors. The results showed that, the number of patients with CSMBS coverage receiving specific COX II inhibitors were greater than the others ($P<0.0001$).

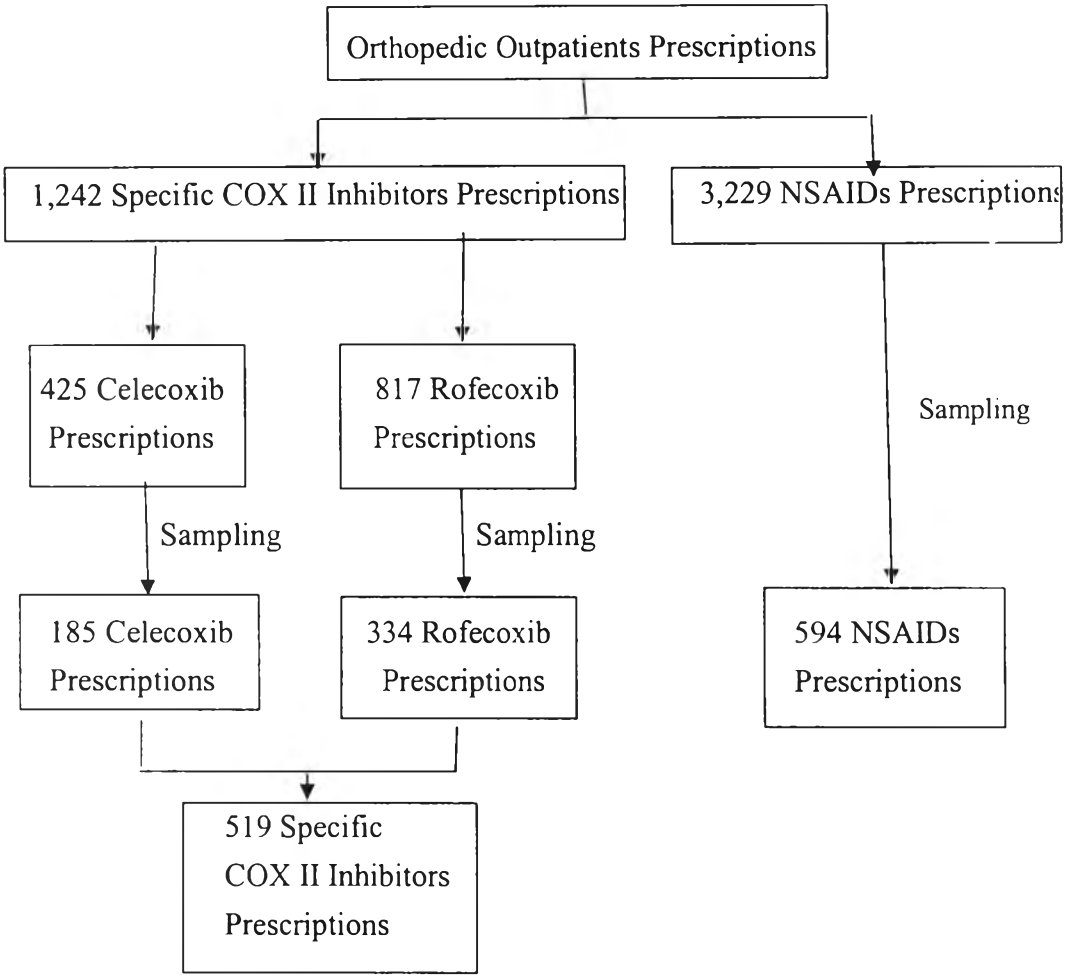


Figure 4.1: The Number of Specific COX II inhibitors Prescriptions and NSAIDs Prescriptions during November 2002 to December 2002 of Orthopedic Outpatients at Lerdsin Hospital.

Table 4.1: Characteristics of Patients Prescribed Specific COX II Inhibitors and NSAIDs.

| Patients' Characteristics | | COX II Inhibitors (N =519) | | NSAIDs (N = 594) | |
|---|---|---|---|---|---|
| | | No. of Pres. | % | No. of Pres. | % |
| Gender | Female | 427 | 82.27 | 394 | 66.33 |
| | Male | 92 | 17.73 | 200 | 33.67 |
| Age | < 65 Years | 337 | 64.93 | 503 | 84.68 § |
| | ≥ 65 Years | 182 | 35.07 | 91 | 15.32 |
| Marital Status | Married | 324 | 62.43 | 327 | 55.05 |
| | Divorced | 63 | 12.14 | 43 | 7.24 |
| | Single | 56 | 10.79 | 136 | 22.9 |
| | Widow | 10 | 1.93 | 13 | 2.19 |
| | Monk, Novice | 2 | 0.39 | 3 | 0.51 |
| | Did not report | 64 | 12.33 | 72 | 12.12 |
| Nationality | Thai | 502 | 96.72 | 589 | 99.16 |
| | Chinese | 16 | 3.08 | 4 | 0.67 |
| | India | 1 | 0.19 | 1 | 0.17 |
| Religion | Buddhism | 502 | 96.72 | 569 | 95.79 |
| | Christ | 12 | 2.31 | 11 | 1.85 |
| | Muslim / Hindu | 5 | 0.96 | 14 | 2.36 |
| Occupation | House Wife / Work at home | 139 | 26.78 | 108 | 18.18 |
| | Civil Servant | 82 | 15.8 | 33 | 5.56 |
| | Sale man | 63 | 12.14 | 54 | 9.09 |
| | Company Officer | 25 | 4.82 | 77 | 12.96 |
| | General Employee | 24 | 4.62 | 143 | 24.07 |
| | Retired Civil Servant | 17 | 3.28 | 6 | 1.01 |
| | State Enterprise Employee | 11 | 2.12 | 19 | 3.20 |
| | Student | 6 | 1.16 | 17 | 2.86 |
| | Farmer | 5 | 0.96 | 9 | 1.52 |

Table 4.1: (Cont.)

| Patients' Characteristics | | COX II Inhibitors (N = 519) | | NSAIDs (N = 594) | |
|---|---|---|---|---|---|
| | | No. of Pres. | % | No. of Pres. | % |
| Occupation | Own Business | 3 | 0.58 | 3 | 0.51 |
| | Private Teacher | 2 | 0.39 | 3 | 0.51 |
| | Government Officer | 1 | 0.19 | 5 | 0.84 |
| | Did not have occupation | 16 | 3.08 | 10 | 1.68 |
| | Did not report | 125 | 24.08 | 107 | 18.01 |
| Payment Status | Out of Pocket | 294 | 56.64 | 353 | 59.43 |
| | Civil Servant MBS* | 152 | 29.29 | 74 | 12.46 § |
| | State Enterprise MBS | 43 | 8.29 | 16 | 2.69 |
| | Social Security Scheme | 10 | 1.93 | 90 | 15.15 |
| | Private Health Insurance | 7 | 1.35 | 2 | 0.34 |
| | MWS** For Veterans | 5 | 0.96 | 2 | 0.34 |
| | Health Card Scheme | 4 | 0.77 | 5 | 0.84 |
| | Elderly uninsured | 2 | 0.39 | 3 | 0.51 |
| | MWS For Religious Leaders | 2 | 0.39 | 3 | 0.51 |
| | Universal Coverage | 0 | 0 | 40 | 6.73 |
| | MWS For Community Leaders | 0 | 0 | 2 | 0.34 |
| | MWS For The Handicapped | 0 | 0 | 2 | 0.34 |
| | Foreign Employee | 0 | 0 | 2 | 0.34 |

* MBS : Medical Benefit Scheme

** MWS : Medical Welfare Scheme

§ $p<0.0001$

**Pattern of drug use**

Of all the orthopedic patients using specific COX II inhibitors, 215 (41.4%) of patients received specific COX II inhibitors plus analgesic drugs or specific COX II inhibitors plus analgesic plus other drugs including 15.6% of patients receiving specific COX II inhibitors plus analgesic drugs and 3.7% of specific COX II inhibitors plus analgesic drugs plus analgesic/anti-inflammatory balm. Specific COX II inhibitors plus gastroprotective drugs (GPAs) plus or specific COX II inhibitors plus GPAs plus other drugs were taken by 159 patients (30.6%) including 87 (7.8%) received specific COX II inhibitors plus GPAs plus analgesic drugs, 45 (4.0%) received specific COX II inhibitors plus GPAs, 15 received specific COX II inhibitors plus GPAs plus analgesic drugs plus analgesic/anti-inflammatory balm (1.4%), 7 (0.6%) received specific COX II inhibitors plus GPAs plus analgesic/anti-inflammatory balm and 3 (0.3%) received specific COX II inhibitors plus GPAs plus NSAIDs injections. One hundred twelve (21.6%) received specific COX II inhibitors alone including celecoxib (6.4%) and rofecoxib (15.2%). Specific COX II inhibitors plus analgesic / anti-inflammatory balm were taken by 19 patients (3.7%). Fourteen of orthopedic outpatients were dispensed specific COX II inhibitors plus NSAIDs injection or specific COX II inhibitors plus NSAIDs injection plus others drugs including 6 (0.5%) received specific COX II inhibitors plus NSAIDs injection plus analgesic drugs, 5 (0.4%) received specific COX II inhibitors plus NSAIDs injection plus analgesic drugs plus analgesic/anti-inflammatory balm and 3 (0.3%) received specific COX II inhibitors plus NSAIDs injection. The results of orthopedic physicians prescribing were depicted in Table 4.2.

Concerning pattern of NSAIDs use, 289 patients receiving NSAIDs plus GPA or NSAIDs plus GPA plus other drug including 177 (15.9%) were prescribed NSAIDs plus GPAs and analgesic drugs, 67 (6.0%) were prescribed NSAIDs plus GPAs, 29 (2.6%) were prescribed NSAIDs plus GPAs plus analgesic drugs plus analgesic/ anti-inflammatory balm, 4 (0.4%) were prescribed NSAIDs plus gastroprotective drugs plus NSAIDs injections plus analgesic drugs, 1 (0.1%) were prescribed NSAIDs plus gastroprotective drugs plus NSAIDs injections plus analgesic/ anti-inflammatory balm, and 1 (0.1%) were prescribed NSAIDs plus gastroprotective drugs plus NSAIDs injections. Two hundred twenty-seven patients (38.2%) received NSAIDs plus analgesic

or NSAIDs plus analgesic plus other drugs including 183 (16.4%) received NSAIDs plus analgesic drugs, 38(3.4%) received NSAIDs plus analgesic drugs plus analgesic / anti-inflammatory balm and 6 ( 0.5%) received NSAIDs plus analgesic drugs plus NSAIDs injection. Sixty seven (11.3%) of patients were dispensed NSAID alone. Eight patients (1.4%) were prescribed NSAIDs plus analgesic/anti-inflammatory balm. Only 3 patients were prescribed two NSAIDs (See Table 4.2).

Table 4.2: Number of Prescriptions based on Pattern of Drugs Use

| | Drug | Number of Prescriptions | % |
|---|---|---|---|
| COX II Inhibitors (N = 519) | COX II + Analgesic or COX II + Analgesic + Other* | 215 | 41.43 |
| | COX II + GPA or COX II + GPA + Other | 159 | 30.64 |
| | COX II Alone | 112 | 21.58 |
| | COX II + Analgesic/Antiiflammatory Gel | 19 | 3.66 |
| | COX II + NSAIDs Injection or COX II + NSAIDs Injection + Other | 14 | 2.70 |
| NSAIDs ( N = 594) | NSAIDs + GPA or NSAIDs +GPA + Other | 289 | 48.65 |
| | NSAIDs + Analgesic or NSAIDs + Analgesic + Other | 227 | 38.22 |
| | NSAIDs Alone | 67 | 11.28 |
| | NSAIDs + Analgesic/Antiiflammatory Gel | 8 | 1.35 |
| | NSAIDs + NSAIDs | 3 | 0.51 |

* Drugs were not Gastroprotective Agents

**Duration of Therapy**

1.1 Duration of Therapy

Specific COX II inhibitors were most frequently prescribed for ≥29 days, followed by 15 to 21 days, 8 to 14 days, ≤7 days, and 22 to 28 days while NSAIDs were most frequently prescribed for between 15 to 21 days followed by ≥29 days, 8 to 14 days, ≤7 days and 22-28 days. (See Table 4.3)

1.2 Mean and Median Duration

Mean duration ± S.D. of three therapies from medical records were presented in Table 4.4 including 31.17 ± 20.35 days for celecoxib use, 27.24 ± 17.45 days for rofecoxib use and 21.36 ± 14.47 days for NSAIDs. Total prescriptions for NSAIDs were 594 for one drug, but there were 3 prescriptions for two NSAIDs. Number of prescriptions of NSAIDs use was 597 prescriptions. Because of right skewed distribution, median would be used instead of mean for the three drugs including piroxicam 10 mg, synflex® 275 mg and clinoril® 150 mg. (51)

Table 4.3: Duration of therapy in patients prescribed Celecoxib, Rofecoxib and NSAIDs

| Drug | ≤7 Days | | 8 to14 Days | | 15 to 21 Days | | 22 to28 Days | | ≥29 days | |
|---|---|---|---|---|---|---|---|---|---|---|
| | No. of Pres. | % | No. of Pres. | % | No. of Pres. | % | No. of. Pres. | % | No. of Pres. | % |
| Celecoxib (N = 185) | 5 | 2.7 | 16 | 8.7 | 59 | 31.9 | 1 | 0.5 | 104 | 56.2 |
| Rofecoxib (N = 334) | 7 | 2.1 | 48 | 14.4 | 108 | 32.3 | 5 | 1.5 | 166 | 49.7 |
| NSAIDS (N = 594) | 51 | 8.6 | 115 | 19.4 | 232 | 39.1 | 4 | 0.7 | 192 | 32.3 |

Table 4.4: Minimum, Maximum, Median and Mean Duration of Specific COX II Inhibitors and NSAIDs therapy during November and December 2002.

| Drug Groups | Drug Names | N | Min. (days) | Max. (Days) | Median (Days) | Mean (Days) | Standard Deviation |
|---|---|---|---|---|---|---|---|
| SC2I | Celecoxib 200 mg | 185 | 5 | 120 | 30 | 31.17 | 20.35 |
| (N=519) | Rofecoxib 25 mg | 334 | 5 | 90 | 25 | 27.24 | 17.45 |
| NSAIDs | Naproxen 250 mg | 5 | 15 | 60 | 30 | 34.00 | 20.43 |
| (N=597) | Sotilen® 20 mg | 10 | 15 | 60 | 25 | 30.50 | 17.55 |
| | Loxonin® 60 mg | 3 | 30 | 30 | 30 | 30.00 | 0 |
| | Brexin® 20 mg | 18 | 5 | 90 | 20 | 26.39 | 24.38 |
| | Reliflex® 500 mg | 18 | 7 | 45 | 30 | 26.36 | 9.92 |
| | Mobic® 75 mg | 85 | 7 | 60 | 20 | 25.55 | 14.60 |
| | Indomethacin 25 mg | 29 | 7 | 120 | 20 | 25.37 | 21.88 |
| | Nidol® 100 mg | 51 | 10 | 60 | 20 | 23.43 | 11.94 |
| | Ibuprofen 400 mg | 21 | 7 | 90 | 15 | 23.02 | 20.37 |
| | Ibuprofen 200 mg | 5 | 3 | 60 | 15 | 23.00 | 23.11 |
| | Voltaren® 25 mg | 43 | 7 | 150 | 15 | 22.75 | 24.70 |
| | Synflex® 275 mg | 37 | 7 | 65 | 20 | 26.58 | 18.40 |
| | Diclofenac 25 mg | 222 | 5 | 120 | 15 | 18.72 | 13.82 |
| | Tilcotil® 20 mg | 11 | 10 | 30 | 15 | 16.27 | 5.55 |
| | Piroxicam 10 mg | 21 | 7 | 60 | 15 | 22.18 | 15.81 |
| | Clinoril® 150 mg | 10 | 5 | 60 | 14.5 | 21.10 | 18.24 |
| | Flogofenac Retard 100 mg | 2 | 10 | 15 | 12.5 | 12.50 | 3.54 |
| | Dolobid® 250 mg | 2 | 7 | 15 | 11 | 11.00 | 5.66 |
| | Ponstan® 250 mg | 4 | 5 | 15 | 5 | 7.50 | 5.00 |
| | All Classical NSAIDs | 597 | 3 | 150 | 18.32 | 21.36 | 14.47 |

**Indications for use**

Concerning the indications for use of specific COX II inhibitors and NSAIDs, Celecoxib was most frequently prescribed for acute pain (36.9%), followed in order by osteoarthritis (26.7%), arthropathy (18.5%), rheumatoid arthritis (6.7%), gouty arthritis (6.7%), chronic pain (2.1%), osteoporosis (1.5%) and arthritis (1.0%). Rofecoxib was most frequently prescribed for acute pain 160 prescriptions (46.1%), followed in order by osteoarthritis (29.7%), arthropathy (9.2%), rheumatoid arthritis (6.3%), gouty arthritis (3.2%), arthritis (3.2%), osteoporosis (1.7%) and chronic pain (0.6%). NSAIDs was most frequently prescribed for acute pain (56.9%), followed in order by osteoarthritis (16.4%), arthropathy (10.9%), gout (5.2%), arthritis (5.2%), rheumatoid arthritis (3.9%), chronic pain (1.0%), and osteoporosis (0.7%).

Arthritis comprised diagnoses of polyarthritis, infectous arthritis and PF arthritis (Plantar Flexion Arthritis) and other arthritis.

Arthropathy included diagnoses of L-spondylolisthesis, spondyloarthropathy, spondylosis, ankylosing spondylosis, spinal stenosis, seronegative arthropathy, and psoriasis arthropathy (51).

Acute pain comprised diagnoses of myalgia, sprain, strain, neuralgia, tendinitis, soft tissue injuries, pelvic pain, menstrual pain, myofascitis, mastalgia, trigger pain, orthopedic fracture, and etc.

Chronic pain was categorized into two group including cancer pain and non cancer pain (52). In this study, cancer pain included R/O TB-malignoma and non cancer pain included TB spine, R/O TB plasma, TB wrist, TB synovitis wrist and R/O TB hip. Some patient had TB with arthritis and Carpal Tunnel Syndrome (CTS) wrist.

The result of indications for use of specific COX II inhibitors and NSAIDs was depicted as shown in Table 4.5.

Table 4.5: Number of Prescriptions based on the Indications by type of NSAIDs use.

| Indications* | Celecoxib | | Rofecoxib | | NSAIDs | |
|---|---|---|---|---|---|---|
| | No.of prescriptions | % | No.of prescriptions | % | No.of prescriptions | % |
| Acute Pain | 65 | 33.33 | 144 | 41.50 | 336 | 54.46 |
| Osteoarthritis | 52 | 26.67 | 103 | 29.68 | 101 | 16.37 |
| Arthropathy | 36 | 18.46 | 30 | 8.64 | 62 | 10.05 |
| Rheumatoid Arthritis | 13 | 6.67 | 22 | 6.34 | 24 | 3.89 |
| Gout | 13 | 6.67 | 11 | 3.17 | 32 | 5.19 |
| Combined Acute Pain | 7 | 3.59 | 16 | 4.61 | 15 | 2.43 |
| Chronic Pain | 4 | 2.05 | 2 | 0.58 | 6 | 0.97 |
| Osteoporosis | 3 | 1.54 | 6 | 1.73 | 4 | 0.65 |
| Arthritis | 2 | 1.02 | 11 | 3.17 | 32 | 5.19 |
| Combined Arthropathy | 0 | 0 | 2 | 0.58 | 5 | 0.81 |
| Total | 195 | 100 | 347 | 100 | 617 | 100 |

*One patient had one or more than one indication

**High Risk Factors**

High risk factors of gastrointestinal complications in patients treated with NSAIDs, can be classified into five categories including age ≥65 years, gastrointestinal and gastroduodenal ulcer or bleeding histories, concomitant use of certain medications, serious co-morbidities, and requirement for the prolonged use of maximum recommended doses of standard NSAIDs (2).

In this study, one patient could have greater than one high risk factor. The results of frequencies of high risk factors of gastrointestinal complications in patients

were depicted in Table 4.6. The high risk factor of gastrointestinal complications in patients was described as follows:

1. Age

Forty percent of patients receiving celecoxib, 32% of patients receiving rofecoxib and 15% of patients receiving NSAIDs aged 65 years and over.

2. Gastrointestinal and gastroduodenal histories

Based on table 4.6, one patient had one or more comorbidities of GI histories, the following data reported the number of patient had GI history. Three patients (1.6%) of receiving celecoxib had gastrointestinal and gastroduodenal histories, 7 patients (2.1%) of receiving rofecoxib had gastrointestinal and gastroduodenal symptoms and 6 patients (1%) of receiving NSAIDs had clinical gastrointestinal and gastroduodenal histories.

Patients receiving celecoxib had gastroduodenal ulcer only one patient, patients receiving rofecoxib had gastroduodenal ulcer 4 patients, and patients receiving NSAIDs had gastroduodenal ulcer 6 patients.

One patient prescribed celecoxib had gastrointestinal surgery at Siriraj Hospital. No patients prescribed rofecoxib or NSAIDs had gastroduodenal perforation or gastrointestinal bleeding.

3. Concomitant use of medications

Three patients prescribed NSAIDs, used corticosteroid concomitantly, but no patient prescribed specific COX II inhibitors were taking corticosteroids. No patients were coprescribed anticoagulant with specific COX II inhibitors or NSAIDS prescribed. Only two patients prescribed rofecoxib low dose aspirin alone concomitantly, no patient was prescribed paediatric aspirin with rofecoxib or NSAIDs. Only six patients prescribed NSAIDs antidiabetes drug alone, no patient was prescribed antidiabetes drug alone with specific COX II inhibitors concomitantly. Three patients prescribed celecoxib, were coprescribed cardiovascular medication, 1 patient prescribed rofecoxib and 1 patient prescribed NSAIDs, used cardiovascular drugs concomitantly. Eighteen patients prescribed rofecoxib, used antihypertensive drugs, 15 patients prescribed NSAIDs and 9 patients prescribed celecoxib. Five patients prescribed rofecoxib, were coprescriped antihypertensive drug and antidiabetes drug, 4 patients prescribed celecoxib and 4

patients prescribed NSAIDs, used antihypertensive drug and antidiabetes drug concomitantly. Only two patients prescribed rofecoxib, were coprescribed antidiabetes drug plus antihypertensive drug plus cardiovascular drug and only 1 patient prescribed NSAIDs, used antidiabetes drug plus antihypertensive drug plus cardiovascular drug concomitantly. For rofecoxib prescriptions, one patient used low dose aspirin plus antidiabetes drugs plus antihypertensive drugs, one patient used low dose aspirin plus cardiovascular drugs plus antihypertensive drugs plus antidiabetes drugs, one patient used low dose aspirin plus antihyperlipidemic drugs and one patient used low dose aspirin with postmenopausal drugs. Of 3 patients received NSAIDs, used multiple concomitantly including one patient on low dose aspirin plus antidiabetes drugs and one patient on low dose aspirin plus cardiovascular drugs plus antihypertensive drugs. Only one patient prescribed celecoxib used low dose aspirin plus cardiovascular drugs and only one patient prescribed celecoxib used antihypertensive drug plus cardiovascular drug.

4. Serious co-morbidities

Four patients prescribed celecoxib had cardiovascular disease alone, one patient prescribed rofecoxib and no patient prescribed NSAIDs. Seven patients prescribed NSAIDs had diabetes mellitus disease alone, 6 prescribed rofecoxib and 2 prescribed celecoxib had diabetes mellitus alone. Eighteen patients prescribed rofecoxib had hypertension alone, 15 patients prescribed NSAIDs and 9 patients prescribed celecoxib had hypertension alone. Only two patients prescribed NSAIDs had renal impairment. No patient who prescribed specific COX II inhibitors had renal impairment. One patient prescribed rofecoxib had hepatic impairment and one patient prescribed NSAIDs had hepatic impairment. Four patients prescribed celecoxib had diabetes mellitus plus hypertension and one patient prescribed celecoxib had hypertension plus cardiovascular disease. Six patients prescribed rofecoxib had diabetes mellitus plus hypertension and 3 patients had diabetes mellitus plus hypertension plus cardiovascular disease. For patient prescribed NSAIDs, 4 patients had diabetes mellitus plus hypertension, one patient had diabetes mellitus plus hypertension plus cardiovascular disease, one patient had hypertension plus cardiovascular disease, one patient had cardiovascular disease plus diabetes mellitus plus renal impairment and one patient had cardiovascular disease plus diabetes mellitus plus hypertension plus renal impairment.

5. Requirement for the prolonged use of maximum recommended doses of standard NSAIDs

Patients who received specific COX II inhibitors or NSAIDs had no indication of use related to the prolonged use of maximum recommended doses of standard NSAIDs. Although severe OA and RA could be consider to warrant high doses for a prolonged duration.

Table 4.6: Number of Patients who had High Risk Factors of Gastrointestinal Complications by Type of NSAIDs*

| | Categories | Celecoxib (N = 185) | | Rofecoxib (N = 334) | | NSAIDs (N = 594) | |
|---|---|---|---|---|---|---|---|
| | | No. of Pres. | % | No. of Pres. | % | No. of Pres. | % |
| Age | ≥ 65 years | 75 | 40.5 | 107 | 32 | 91 | 15.3 |
| GI History | Gastroduodenal ulcer | 2 | 1.1 | 7 | 2.1 | 6 | 1.0 |
| | Gastrointestinal bleeding or Gastroduodenal perforation | 1 | 0.5 | 0 | 0 | 0 | 0 |
| | Total GI History | (3) | (1.6) | (7) | (2.1) | (6) | (1.0) |
| Comedication | Corticosteroid | 0 | 0 | 0 | 0 | 3 | 0.5 |
| | Anticoagulant | 0 | 0 | 0 | 0 | 0 | 0 |
| | Low Dose Aspirin | 0 | 0 | 2 | 0.6 | 0 | 0 |
| | Antidiabetes Drugs | 0 | 0 | 0 | 0 | 6 | 1.0 |
| | Cardiovascular Drugs | 3 | 1.6 | 1 | 0.3 | 1 | 0.2 |
| | Antihypertensive Drugs | 9 | 4.9 | 18 | 5.4 | 15 | 2.5 |
| | Combined Drugs | | | | | | |
| | HT[¶] + DM[†] Drugs | 4 | 2.2 | 5 | 1.5 | 4 | 0.7 |
| | HT + DM + CVS[‡] Drugs | 0 | 0 | 2 | 0.6 | 1 | 0.2 |
| | HT + CVS Drugs | 1 | 0.5 | 0 | 0 | 0 | 0 |
| | ASA[§]+ DM Drugs | 0 | 0 | 0 | 0 | 1 | 0.2 |
| | ASA+ CVS Drugs | 1 | 0.5 | 0 | 0 | 1 | 0.2 |
| | ASA+ CVS+ HT Drugs | 0 | 0 | 0 | 0 | 1 | 0.2 |
| | ASA+ DM + HT Drugs | 0 | 0 | 1 | 0.3 | 0 | 0 |
| | ASA+ CVS+ HT+DM Drugs | 0 | 0 | 1 | 0.3 | 1 | 0.2 |
| | Total Comedication | (18) | (9.7) | (30) | (9.0) | (34) | (5.7) |

Table 4.6: (Cont.)

| | Categories | Celecoxib (N = 185) | | Rofecoxib (N = 334) | | NSAIDs (N = 594) | |
|---|---|---|---|---|---|---|---|
| | | No. of Pres. | % | No. of Pres. | % | No. of Pres. | % |
| Comorbidities | Cardiovascular Disease | 4 | 2.2 | 1 | 0.3 | 0 | 0 |
| | Diabetes Mellitus | 2 | 1.1 | 6 | 1.8 | 7 | 1.2 |
| | Hypertension | 9 | 4.9 | 18 | 5.4 | 15 | 2.5 |
| | Renal Impairment | 0 | 0 | 0 | 0 | 0 | 0 |
| | Hepatic Impairment | 0 | 0 | 1 | 0.3 | 1 | 0.2 |
| | Combined Disease | | | | | | |
| | DM + HT | 4 | 2.2 | 6 | 1.8 | 4 | 0.7 |
| | HT + CVS | 1 | 0.5 | 0 | 0 | 1 | 0.2 |
| | CVS + Renal Impairment | 0 | 0 | 0 | 0 | 1 | 0.2 |
| | DM + HT + CVS | 0 | 0 | 3 | 0.9 | 1 | 0.2 |
| | DM + HT + Renal | 0 | 0 | 0 | 0 | 1 | 0.2 |
| | CVS + DM + Renal | 0 | 0 | 0 | 0 | 1 | 0.2 |
| | CVS + DM + HT + Renal | 0 | 0 | 0 | 0 | 1 | 0.2 |
| | Total Comorbidities | (20) | (10.8) | (35) | (10.5) | (33) | (5.6) |
| Prolong use** | | 0 | 0 | 0 | 0 | 0 | 0 |

* One patient had one or more than categories of high risk factors

** Prolonged use of maximum recommended doses of standard NSAIDs

† DM : Antidiabetes drug, ‡ CVS : Cardiovascular Drug, ¶ HT : Antihypertensive Drugs, § ASA: Aspirin

**High Risk and Low Risk Ratio**

Using The National Institute of Center of Excellence (NICE) of United Kingdom Guidance for specific COX II inhibitors to determine whether patients receiving specific COX II inhibitors were at high risk, the data concerning number and percent of high risk and low risk were reported in the following. Of a total of 185 prescriptions for celecoxib, 104 (56.22%) prescriptions were for patients in a low risk group and 81 prescriptions (43.78%) were for patients in a high risk group. Of a total 334 patients for rofecoxib, 207 (61.98%) prescriptions were for patients in low risk group and 127 prescriptions (38.02%) were for patients in the high risk group. Of a total of 594 prescriptions for NSAIDs, 481 prescriptions (80.98%) were for patients in low risk group and 113 prescriptions (19.02%)

were for patients in the high risk group. The results of number of prescriptions in low risk and high risk group of specific COX II inhibitors and NSAIDs using are illustrated in Figure 4.2. Table 4.7 shows number and percentages for patients in the low risk and high risk groups for patients taking NSAIDs and specific COX II inhibitors.

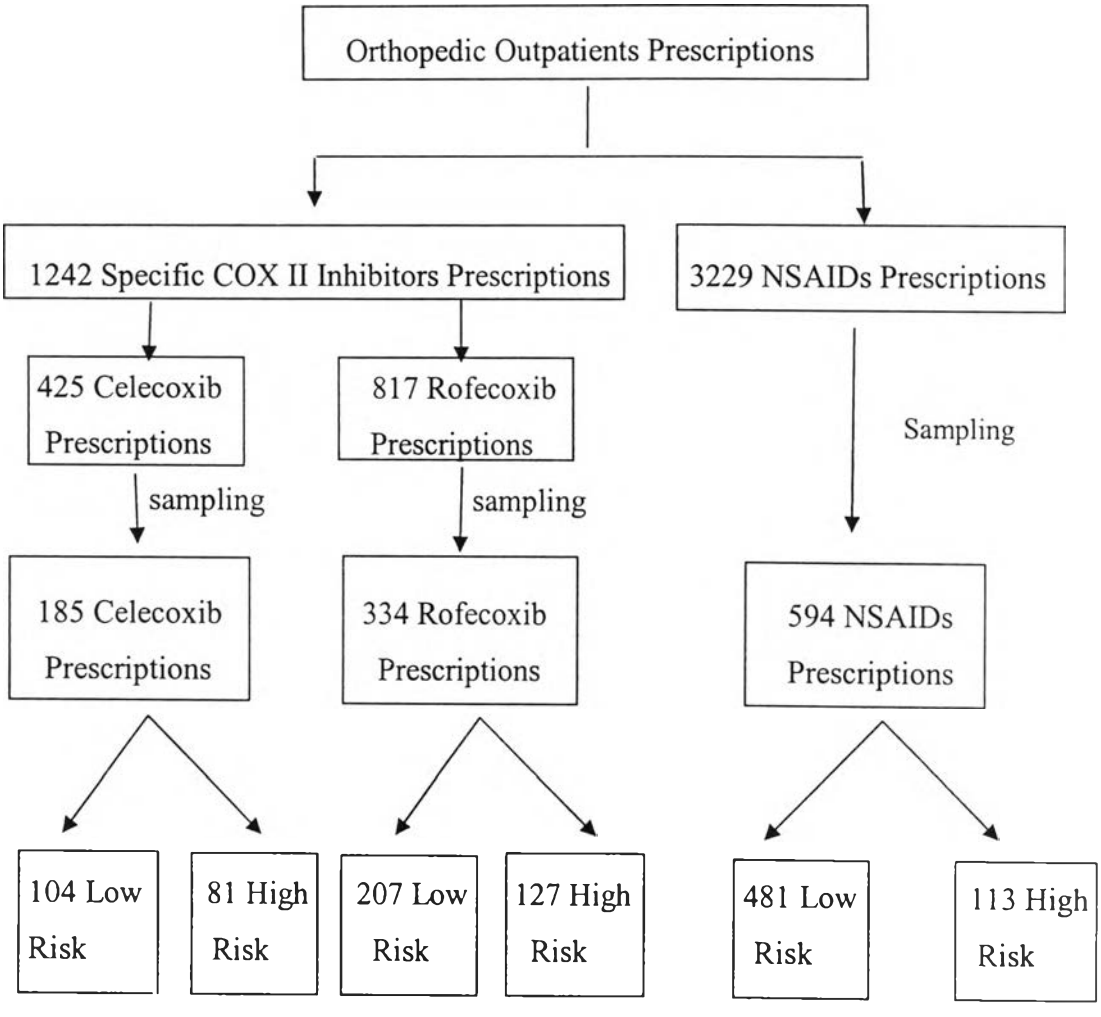


Figure 4.2: Number of prescriptions in low risk and high risk of specific COX II inhibitors and NSAIDs using.

Table 4.7: Number of Prescriptions in Low Risk and High Risk for Upper GI Adverse Effects of Specific COX II Inhibitors and NSAIDs Using during November 2002 to December 2002 of Orthopedic Outpatients at Lerdsin Hospital.

| Group | Celecoxib (N = 185) | | Rofecoxib (N = 334) | | NSAIDs (N = 594) | |
|---|---|---|---|---|---|---|
| | No.of Prescriptions | % | No.of Prescriptions | % | No.of Prescriptions | % |
| Low risk | 104 | 56.22 | 207 | 61.98 | 481 | 80.98 |
| High Risk | 81 | 43.78 | 127 | 38.02 | 113 | 19.02 |
| Total | 185 | 100 | 334 | 100 | 594 | 100 |

Data indicated that 56% of the patients receiving celecoxib, (were in low risk group), about 60% of patients receiving rofecoxib, (were in low risk group) and about 80% of patients receiving NSAIDs were in low risk for upper GI adverse events.

The result of pattern of drug use for low risk patients, 311 of patients receiving specific COX II inhibitors were inappropriate use. One hundred thirteen of patient receiving NSAIDs for high risk group were inappropriate use.

For pattern of specific COX II inhibitors use, they are not recommended for routine use in patients with RA or OA. They should be used, in preference to standard NSAIDs based on NICE guidance. From this study, patients who received specific COX II inhibitors first time use was about 33.3%. Physician prescribed appropriate specific COX II inhibitors use in low risk group was 59.92%.

**Cost Waste**

1.1 Cost Waste for Patients in Low Risk Groups

1.1.1 Cost Waste for Patients in Low Risk Groups of Actual Practice

$$\text{Average Cost Per Prescription} = \frac{\text{Total Cost}}{\text{Number of Prescriptions}}$$

For actual practice, total cost of celecoxib use was 88,584.96 Baht, total cost of rofecoxib use was 149,710.41 Baht and total cost of NSAIDs use was 79,520.61 Baht in low risk group. Number of low risk of celecoxib use, rofecoxib use and NSAIDs use were described in Table 4.7. From this study, average cost per prescription for celecoxib was 851.78 Baht, 723.24 Baht for rofecoxib and 165.32 Baht for NSAIDs in low risk group. The results of total cost and cost per prescription in low risk group of specific COX II inhibitors and NSAIDs use are shown in Table 4.8. Average cost per prescription was calculated by the following formula:

$$\text{Average Cost Per Prescription}_{\text{Celecoxib}} = \frac{88,584.96}{104} = 851.78 \text{ Baht}$$

$$\text{Average Cost Per Prescription}_{\text{Rofecoxib}} = \frac{149,710.41}{207} = 723.24 \text{ Baht}$$

$$\text{Average Cost Per Prescription}_{\text{NSAIDs}} = \frac{79,520.61}{481} = 165.32 \text{ Baht}$$

Table 4.8: Total Cost and Average Cost per Prescription of Specific COX II Inhibitors and NSAIDs Use in Low Risk and High Risk Group.

| Drug Name | Low Risk Group | | | High Risk Group | | |
|---|---|---|---|---|---|---|
| | N | Total Cost (Baht) | Average Cost per Prescription (Baht) | N | Total Cost (Baht) | Average Cost per Prescription (Baht) |
| Rofecoxib | 207 | 149,710.41 | 723.24 | 127 | 118,956.06 | 936.66 |
| Celecoxib | 104 | 88,584.96 | 851.78 | 81 | 77,589.12 | 957.89 |
| Diclofenac | 180 | 466.95 | 2.59 | 42 | 90.00 | 2.14 |
| Diclofenac Inj. | 3 | 15.00 | 5.00 | 1 | 5.00 | 5.00 |
| Ponstan® | 3 | 27.50 | 9.17 | 1 | 33.00 | 33.00 |
| Indomethacin | 29 | 334.40 | 11.53 | 0 | 0.00 | 0.00 |
| Ibuprofen(400) | 16 | 206.25 | 12.89 | 5 | 126.25 | 25.25 |
| TA Injection | 11 | 170.40 | 15.49 | 0 | 0.00 | 0.00 |
| Piroxicam | 18 | 297.20 | 16.51 | 3 | 27.20 | 9.07 |
| Ibuprofen(200) | 3 | 52.90 | 17.63 | 2 | 50.60 | 25.30 |
| Flogofenac Retard | 1 | 90.75 | 90.75 | 1 | 60.50 | 60.50 |
| Naproxen | 4 | 399.00 | 99.75 | 1 | 140.00 | 140.00 |
| Dolobid® | 2 | 231.88 | 115.94 | 0 | 0.00 | 0.00 |
| Sotilen® | 8 | 1,317.95 | 164.74 | 2 | 551.70 | 275.85 |
| Tilcotil ® | 7 | 1,247.38 | 178.20 | 4 | 1,127.95 | 281.99 |
| Voltaren® | 38 | 7,905.48 | 208.04 | 5 | 4,000.20 | 800.04 |
| Loxonin® | 2 | 486.00 | 243.00 | 1 | 162.00 | 162.00 |
| Nidol® | 42 | 11,200.00 | 266.67 | 9 | 2,944.00 | 327.11 |
| Clinoril® | 4 | 1376.70 | 344.18 | 6 | 1,567.32 | 261.22 |
| Mobic® | 64 | 24,072.95 | 376.14 | 21 | 9,297.75 | 442.75 |
| Brexin® | 16 | 6,020.00 | 376.25 | 2 | 840.00 | 420.00 |
| Synflex® | 30 | 11,792.33 | 393.08 | 7 | 4,779.50 | 682.79 |
| Reliflex® | 16 | 11,809.59 | 738.10 | 2 | 973.70 | 486.85 |
| All Classical NSAIDs | 481 | 79,520.61 | 165.32 | 113 | 26,776.67 | 236.96 |

However cost per prescription could not account for how many days of drug taken by the patient for each prescription. Average cost per day of specific COX II inhibitors and NSAIDs use in low risk group were calculated. Average cost per day equal average cost per prescription divided by average duration of therapy by the following equation:

$$\text{Average Cost Per Day} = \frac{\text{Average Cost Per Prescription}}{\text{Mean Duration of Therapy}}$$

Average of duration of celecoxib therapy was 31.17 days, 27.24 days for patients receiving rofecoxib and 21.36 days for patients receiving NSAIDs.(Table 4.4). The results found that, average cost per day of celecoxib use was 27.33 Baht and average cost per day of rofecoxib use was 26.55 Baht. Average cost per day of NSAIDs use was 7.74 Baht. The result of average cost per day of specific COX II inhibitors and NSAIDs in low risk group of actual practice are presented in Table 4.9. The results of cost per day of specific COX II inhibitors and NSAIDs use in low risk and high risk group are given in Table 4.10.

Table 4.9 Average Cost per Day of Specific COX II Inhibitors and NSAIDs in Low Risk Group of Actual Practice

| Low risk group of actual practice | Celecoxib | Rofecoxib | NSAIDs |
|---|---|---|---|
| Average Cost per Prescription ( Baht) | 851.78 | 723.24 | 165.32 |
| Mean Duration (Days) | 31.17 | 27.24 | 21.36 |
| Average Cost per Day (Baht) | 27.33 | 26.55 | 7.74 |

Table 4.10: Cost Per Day of Specific COX II Inhibitors and NSAIDs in low risk and high risk group.

| Group | Celecoxib (Baht / Day) | Rofecoxib (Baht / Day) | NSAIDs (Baht / Day) |
|---|---|---|---|
| Low Risk Group | 27.33 | 26.55 | 7.74 |
| High Risk Group | 30.73 | 34.39 | 11.21 |

Total cost waste equal difference cost per day between specific COX II inhibitors and NSAIDs use multiplied by number of patients and multiplied by mean of duration therapy by the following equation:

$$\text{Total Cost Waste}_{\text{Low Risk}} = (C_{\text{COX II}} - C_{\text{NSAIDs}}) * D_{\text{COX II}} * N_{\text{COX II}}$$

; $C_{\text{COX II}}$ = Cost Per Day of Specific COX II Inhibitors Use in Low Risk

$C_{\text{NSAIDs}}$ = Cost Per Day of NSAIDs Use in Low Risk

$D_{\text{COX II}}$ = Average Duration of Specific COX II Inhibitors Use in Low Risk

$N_{\text{COX II}}$ = Number of Patients of Specific COX II Inhibitors Use in Low Risk

The cost difference per day between celecoxib and NSAIDs was 19.59 Baht. Therefore, the total difference in costs per day in 104 patients of receiving celecoxib in low risk group was 2,037.36 Baht. Average duration therapy of receiving celecoxib was 31.17 days (Tabie 4.4). Total cost waste equals the difference cost per day multiplied by average duration therapy. Total cost waste of celecoxib use in low risk group was 63,504.51 Baht in one course therapy by the following equation;

$$\text{Total Cost Waste}_{\text{Celecoxib}} = (27.33 - 7.74) \text{ Baht} * 104 \text{ Patients} * 31.17 \text{ days}$$

$$= 63{,}504.51 \text{ Baht} \quad \_(1)$$

The cost difference per day between rofecoxib and NSAIDs was 18.81 Baht. Therefore, total the difference costs per day in 207 patients of receiving rofecoxib in low risk group were 3,893.67 Baht. Average duration therapy of receiving rofecoxib was 27.24 days (Table 4.4). Total cost waste of rofecoxib use in low risk group was 106,063.57 Baht in one cycle therapy by the following formula:

$$\text{Total Cost Waste}_{\text{Rofecoxib}} = (26.55 - 7.74) \text{ Baht} * 207 \text{ Patients} * 27.24 \text{ days}$$

$$= 106{,}063.57 \text{ Baht} \quad \_(2)$$

Total cost waste of specific COX II inhibitors was total cost waste of celecoxib use plus total cost waste of rofecoxib use in the following equation:

$$\text{Total Cost Waste}_{\text{Specific COX II inhibitors}} = (1) + (2)$$

$$= 63{,}504.51 + 106{,}063.57$$

$$= 169{,}568.08 \text{ Baht}$$

For actual practice, total cost waste of specific COX II inhibitors use in low high risk group compared with NSAIDS use were 169,568.08 Baht.

During the study period, total the celecoxib prescriptions were 425 prescriptions, total the rofecoxib prescriptions were 817 prescriptions and total the NSAIDs prescriptions were 3,229 prescriptions (Figure 4.1). Percentages of low risk and high risk patients of celecoxib use were 56.22 % based on assumption that percentages of low risk per high risk of studying as same as sampling (Table 4.7). The numbers of low risk patients prescribed celecoxib in two months was 239 patients. Difference in costs per day in 239 patients was 4,682.01 Baht. Total cost of one course of celecoxib therapy compared with NSAIDs therapy in low risk group patients was 145,938.25 Baht, calculated by the following equation:

$$\text{Total Cost Waste}_{\text{Celecoxib}} = (27.33 - 7.74)\ \text{Baht} * 239\ \text{Patients} * 31.17\ \text{days}$$
$$= 145{,}938.25\ \text{Baht} \quad \_(3)$$

In the same manner, percentages of low risk and high risk patients of rofecoxib use were 61.98 % (Table 7). The numbers of low risk patients prescribed rofecoxib in two months was 506 patients. Difference in costs per day in 506 patients was 9,517.86 Baht. Total costs of one course rofecoxib therapy compared with NSAIDs therapy in low risk group were 259,266.51 Baht, calculated by the following equation:

$$\text{Total Cost Waste}_{\text{Rofecoxib}} = (26.55 - 7.74)\ \text{Baht} * 506\ \text{Patients} * 27.24\ \text{days}$$
$$= 259{,}266.51\ \text{Baht} \quad \_(4)$$

For two months, total estimated cost waste of specific COX II inhibitors use compared with NSAIDs use in low risk group were 405,204.76 Baht in the following formula:

$$\text{Total Cost Waste}_{\text{Specific COX II inhibitors}} = (3) + (4)$$
$$= 145{,}938.25 + 259{,}266.51$$
$$= 405{,}204.76\ \text{Baht}$$

For one year, total estimated cost waste of specific COX II inhibitors use compared with NSAIDs use in low risk group was 2,431,228.56 Baht, calculated by the following equation:

$$\text{Total cost waste}_{12\ \text{months}} = \text{Total Cost waste}_{2\ \text{months}}\ (\text{Baht}) * 6$$
$$= 405{,}204.76 * 6$$
$$= 2{,}431{,}228.56\ \text{Baht}$$

The result of total estimated cost waste of specific COX II inhibitors use compared with NSAIDs use in low risk group are presented in Table 4.11.

Table 4.11: Total Estimated Cost Waste of Specific COX II Inhibitors Use Compared with NSAIDs Use in Low Risk Group of Actual Practice.

| Actual Practice | Celecoxib | | | | Rofecoxib | | | |
|---|---|---|---|---|---|---|---|---|
| | Difference Cost per Day (Baht)* | No. of Low risk | Average Duration Therapy (Days) | Total Cost (Baht) | Difference Cost per Day (Baht)* | No. of Low risk | Average Duration Therapy (Days) | Total Cost (Baht) |
| Sample | 19.59 | 104 | 31.17 | 63,504.51 | 18.81 | 207 | 27.24 | 106,063.57 |
| 2 months | 19.59 | 239 | 31.17 | 145,938.25 | 18.81 | 506 | 27.24 | 259,266.51 |
| 1 Year | | | | 875,629.50 | | | | 1,555,599.06 |

Note: * Difference Cost per Day Specific COX II Inhibitors Compared With NSAIDs Use in Low Risk Group.

; cost per day $_{celecoxib}$ = 27.33 Baht

cost per day $_{rofecoxib}$ = 26.55 Baht

cost per day $_{NSAIDs}$ = 7.74 Baht

1.1.2 Cost waste in low risk of standard treatment

For standard treatment, drug consumption volume of NSAIDs use in fiscal year 2002 from pharmacy department was collected as presented in Table 4.12.

Table 4.12: Drug Consumption Volume of Specific COX II inhibitors and NSAIDs in Fiscal Year 2002.

| Drug Groups | Drugs Name | Drug Consumption Volume (Tablets) | % |
|---|---|---|---|
| COX II Inhibitors | Celecoxib 200 mg | 116,900 | 39.96 |
| | Rofecoxib 25 mg | 175,620 | 60.04 |
| NSAIDs | Diclofenac 25 mg | 1,095000 | 44.05 |
| | Voltaren® 25 mg | 228,000 | 9.17 |
| | Ibuprofen 400 mg | 205,000 | 8.25 |
| | Indomethacin 25 mg | 150,000 | 6.03 |
| | Synflex® 275 mg | 125,820 | 5.06 |
| | Nidol® 100 mg | 118,000 | 4.75 |
| | Piroxicam 10 mg | 117,500 | 4.73 |
| | Mobic® 75 mg | 106,400 | 4.28 |
| | Ponstan® 250 mg | 76,500 | 3.08 |
| | Ibuprofen 200 mg | 62,000 | 2.49 |
| | Brexin® 20 mg | 48,660 | 1.96 |
| | Reliflex® 500 mg | 38,080 | 1.53 |
| | Naproxen 250 mg | 30,000 | 1.21 |
| | Sotilen® 20 mg | 25,300 | 1.02 |
| | Clinoril® 150 mg | 23,000 | 0.93 |
| | Tilcotil® 20 mg | 12,600 | 0.51 |
| | Dolobid® 250 mg | 10,000 | 0.40 |
| | TA Injection | 5,150 | 0.21 |
| | Flogofenac Retard 100 mg | 4,500 | 0.18 |
| | Loxonin® 60 mg | 2,000 | 0.08 |
| | Diclofenac Injection | 2,070 | 0.08 |

The three highest rank of drug consumption volume of NSAIDs in fiscal year 2002 were diclofenac 25 mg, voltaren® 25 mg and ibuprofen 400 mg, respectively. Diclofenac consumption volume was 1,095,000 tablets (44.1%), voltaren® consumption volume was 228,000 tablets (9.2%) and ibuprofen 400 mg consumption volume was 205,000 tablets (8.3%). (See Table 4.12)

Average duration of diclofenac use was 18.72 days, average duration of voltaren® therapy was 22.75 days and average duration of ibuprofen 400 mg therapy was 23.02 days from this study. (Table 4.4) Acquisition cost of diclofenac was 0.05 Baht per tablet, acquisition cost of voltaren® was 4.52 Baht per tablet and acquisition cost of ibuprofen 400 mg was 0.46 Baht per tablet as presented in Table 4.13.

Average cost per day was Defined Daily Dose (DDD) multiplied by acquisition cost. Cost per day of diclofenac use was 0.15 Baht, cost per day of voltaren® use was 13.56 Baht and cost per day of ibuprofen 400 mg use was 1.38 Baht based on DDD of three drugs equal 1*3 pc of all indication. The results of cost per day of NSAIDs of standard treatment are given in Table 4.14. Average cost per day of NSAIDs in standard treatment was calculated in the following formula:

Average Cost Per Day = Defined Daily Dose * Acquisition Cost

Average Cost Per Day $_{\text{Diclofenac}}$ = 3 * 0.05 = 0.15 Baht

Average Cost Per Day $_{\text{Voltaren®}}$ = 3 * 4.52 = 13.56 Baht

Average Cost Per Day $_{\text{Ibuprofen 400 mg}}$ = 3 * 0.46 = 1.38 Baht

The difference cost per day between celecoxib and diclofenac in standard treatment was 27.18 Baht. Therefore, the total difference in costs per day in 104 patients of receiving celecoxib in low risk group was 2,826.72 Baht. Average duration therapy of receiving celecoxib was 31.17 days (Table 4.4). Total cost waste of celecoxib use compared with diclofenac in low risk group was 88,108.86 Baht in one course therapy of standard treatment.

The difference cost per day between celecoxib and voltaren® in standard treatment was 13.77 Baht. Therefore, the total difference in costs per day in 104 patients of receiving celecoxib in low risk group was 1,432.08 Baht. Average duration therapy of receiving celecoxib was 31.17 days (Table 4.4). Total cost waste of celecoxib use compared with voltaren® use in low risk group was 44,637.93 Baht in one course therapy of standard treatment.

The difference cost per day between celecoxib and ibuprofen 400 mg in standard treatment was 25.95 Baht. Therefore, the total difference in costs per day in 104 patients of receiving celecoxib in low risk group was 2,698.80 Baht. Average duration therapy of receiving celecoxib was 31.17 days (Table 4.4). Total cost waste of celecoxib use compared with ibuprofen 400 mg use in low risk group were 84,121.60 Baht in one course therapy of standard treatment.

The difference cost per day between rofecoxib and diclofenac was 26.40 Baht. Therefore, the total difference costs per day in 207 patients of receiving rofecoxib in low risk group were 5,464.80 Baht. Average duration therapy of receiving rofecoxib was 27.24 days (Table 4.4). Total cost waste of rofecoxib use compared with diclofenac use in low risk group was 148,861.15 Baht in one cycle therapy of standard treatment.

The difference cost per day between rofecoxib and voltaren® was 12.99 Baht. Therefore, the total difference in costs per day in 207 patients of receiving rofecoxib in low risk group was 2,688.93 Baht. Average duration therapy of receiving rofecoxib was 27.24 days (Table 4.4). Total cost waste of rofecoxib use compared with voltaren® use in low risk group was 73,246.45 Baht in one cycle therapy of standard treatment.

The difference cost per day between rofecoxib and ibuprofen 400 mg was 25.17 Baht. Therefore, the total difference in costs per day in 207 patients of receiving rofecoxib in low risk group was 5,210.19 Baht. Average duration therapy of receiving rofecoxib was 27.24 days (Table 4.4). Total cost waste of rofecoxib use

compared with ibuprofen 400 mg use in low risk group were 141,925.58 Baht in one cycle therapy of standard treatment.

For standard treatment, total cost waste of specific COX II inhibitors use in low risk group compared with diclofenac was 236,970.01 Baht. Total cost waste of specific COX II inhibitors use in low risk group compared with voltaren® was 117,884.38 Baht and total cost waste of specific COX II inhibitors use in low risk group compared with ibuprofen 400 mg was 226,047.18 Baht. The result of specific COX II inhibitors use compared with NSAIDs of standard treatment of 1,113 patients is presented in Table 4.15.

During the study period, total the celecoxib prescriptions were 425 prescriptions, total the rofecoxib prescriptions were 817 prescriptions and total the NSAIDs prescriptions were 3,229 prescriptions (Figure 4.1). Percentages of low risk per high risk patients of celecoxib use were 56.22 % based on assumption that percentages of low risk per high risk of studying as same as sampling (Table 4.7). The numbers of low risk patients prescribed celecoxib two months was 239 patients.

The difference in costs per day in 239 patients of receiving celecoxib compared with diclofenac in low risk group patients was 6,496.02 Baht. Total cost of one course of celecoxib therapy compared with diclofenac therapy in low risk group patients for standard treatment was 202,480.94 Baht.

The difference in costs per day in 239 patients of receiving celecoxib compared with voltaren® in low risk group was 3,291.03 Baht. Total cost of one course of celecoxib therapy compared with voltaren® therapy in low risk group for standard treatment was 102,581.41 Baht.

The difference in costs per day in 239 patients of receiving celecoxib compared with ibuprofen 400 mg in low risk group was 6,202.05 Baht. Total cost of one course of celecoxib therapy compared with ibuprofen 400 mg therapy in low risk group for standard treatment was 193,317.90 Baht.

In the same manner, percentages of low risk per high risk patients of rofecoxib use were 61.98 % (Table 4.7). The numbers of low risk patients prescribed rofecoxib during two months was 506 patients. Difference in costs per day in 506 patients of receiving rofecoxib compared with diclofenac was 13,358.40 Baht. Total cost of one course rofecoxib therapy compared with diclofenac therapy in low risk group patients was 363,882.82 Baht.

Difference in costs per day in 506 patients of receiving rofecoxib compared with voltaren® was 6,527.94 Baht. Total cost of one course rofecoxib therapy compared with voltaren® therapy in low risk group was 179,046.89 Baht.

Difference in costs per day in 506 patients of receiving rofecoxib compared with ibuprofen 400 mg was 12,736.02 Baht. Total cost of one course rofecoxib therapy compared with ibuprofen 400 mg therapy in low risk group was 346,929.18 Baht.

For two months, total estimated cost waste of specific COX II inhibitors use compared with diclofenac use in low risk group of standard treatment was 566,363.76 Baht, total estimated cost waste of specific COX II inhibitors use compared with voltaren® use in low risk group of standard treatment was 281,628.30 Baht, and total estimated cost waste of specific COX II inhibitors use compared with ibuprofen 400 mg use in low risk group of standard treatment was 540,247.08 Baht.

For one year, total estimated cost waste of specific COX II inhibitors use compared with diclofenac use in low risk group for standard treatment was 3,398,182.56 Baht, total estimated cost waste of specific COX II inhibitors use compared with voltaren® use in low risk group of standard treatment was 1,689,769.80 Baht and total estimated cost waste of specific COX II inhibitors use compared with Ibuprofen 400 mg use in low risk group for standard treatment was 3,241,482.48 Baht.

The results of total estimated cost waste of specific COX II inhibitors use compared with NSAIDs use in low risk group of standard treatment during two months are presented in Table 4.16.

The results of total estimated cost waste of specific COX II inhibitors use compared with NSAIDs use in low risk group of actual practice and standard treatment among sample under study, overall in 2 months and 1 year was presented in Table 4.17.

Table 4.13: Acquisition cost of Specific COX II Inhibitors and NSAIDs in Fiscal Year 2003 at Lerdsin Hospital.

| Drug Groups | Drugs Name | Acquisition Cost (Baht / Tablet or Ampule) |
|---|---|---|
| COX II Inhibitors | Celecoxib | 22.08 |
| | Rofecoxib | 29.43 |
| NSAIDs | Diclofenac 25 mg | 0.05 |
| | Indomethacin 25 mg | 0.19 |
| | Ibuprofen 200 mg | 0.25 |
| | Piroxicam 10 mg | 0.40 |
| | Ibuprofen 400 mg | 0.46 |
| | Ponstan® 250 mg | 0.55 |
| | Naproxen 250 mg | 1.40 |
| | Voltaren® 25 mg | 4.52 |
| | Diclofenac Injection | 5.00 |
| | Dolobid® 250 mg | 5.27 |
| | Loxonin® 60 mg | 5.40 |
| | Flogofenac Retard 100 mg | 6.05 |
| | Sotilen® 20 mg | 6.13 |
| | Nidol® 100 mg | 6.40 |
| | Clinoril® 150 mg | 7.06 |
| | Synflex® 275 mg | 8.69 |
| | Mobic® 75 mg | 12.65 |
| | Tilcotil® 20 mg | 13.27 |
| | Reliflex® 500 mg | 13.91 |
| | Brexin® 20 mg | 14.00 |
| | TA Injection | 14.20 |

Table 4.14: Cost per Day of NSAIDs Standard Treatment

| Group | Diclofenac (Baht / Day) | Voltaren® (Baht / Day) | Ibuprofen 400 mg (Baht / Day) |
|---|---|---|---|
| Low risk and high risk group | 0.15 | 13.56 | 1.38 |

Table 4.15: Total cost waste of Specific COX II Inhibitors use compared with NSAIDs Standard Treatment of 1,113 patients.

| | Celecoxib | | | | Rofecoxib | | | |
|---|---|---|---|---|---|---|---|---|
| Standard Treatment (N=1,113) | No. of Low risk | Average Duration Therapy (Days) | Difference Cost per Day (Baht)* | Total Cost (Baht) | No. of Low risk | Average Duration Therapy (Days) | Difference Cost per Day (Baht)* | Total Cost (Baht) |
| Diclofenac | 104 | 31.17 | 27.18 | 88,108.86 | 207 | 27.24 | 26.40 | 148,861.15 |
| Voltaren® | 104 | 31.17 | 13.77 | 44,637.93 | 207 | 27.24 | 12.99 | 73,246.45 |
| Ibuprofen 400 mg | 104 | 31.17 | 25.95 | 84,121.60 | 207 | 27.24 | 25.17 | 141,925.58 |

* Difference Cost per Day Specific COX II inhibitors Compared With NSAIDs Use in Low Risk Group.
; cost per day $_{Celecoxib}$ = 27.33 Baht
cost per day $_{Rofecoxib}$ = 26.55 Baht
cost per day $_{Diclofenac}$ = 0.15 Baht
cost per day $_{Voltaren}$ = 13.56 Baht
cost per day $_{Ibuprofen\ 400\ mg}$ = 1.38 Baht

Table 4.16: Total cost waste of Specific COX II Inhibitors use compared with NSAIDs Standard Treatment of two months.

| Standard Treatment (2 month) | Celecoxib | | | | Rofecoxib | | | |
|---|---|---|---|---|---|---|---|---|
| | No. of Low risk | Average Duration Therapy (Days) | Difference Cost per Day (Baht)* | Total Cost (Baht) | No. of Low risk | Average Duration Therapy (Days) | Difference Cost per Day (Baht)* | Total Cost (Baht) |
| Diclofenac | 239 | 31.17 | 27.18 | 202,480.94 | 506 | 27.24 | 26.40 | 363,882.82 |
| Voltaren® | 239 | 31.17 | 13.77 | 102,581.41 | 506 | 27.24 | 12.99 | 179,046.89 |
| Ibuprofen 400 mg | 239 | 31.17 | 25.95 | 193,317.90 | 506 | 27.24 | 25.17 | 540,247.08 |

* Difference Cost per Day Specific COX II Inhibitors Compared With NSAIDs Use in Low Risk Group.
; cost per day $_{Celecoxib}$ = 27.33 Baht
cost per day $_{Rofecoxib}$ = 26.55 Baht
cost per day $_{Diclofenac}$ = 0.15 Baht
cost per day $_{Voltaren}$ = 13.56 Baht
cost per day $_{Ibuprofen\ 400\ mg}$ = 1.38 Baht

Table 4.17: Total Estimated Cost Waste of Specific COX II Inhibitors Use Compared with NSAIDs in Low Risk Group of Actual Practice and Standard Treatment.

| Study | Actual Practice | Standard Treatment | | |
|---|---|---|---|---|
| | Specific COX II Inhibitors vs NSAIDs | Specific COX II Inhibitors vs Diclofenac | Specific COX II Inhibitors vs Voltaren® | Specific COX II Inhibitors vs Ibuprofen (400) |
| Sample | 169,568.08 | 236,970.01 | 117,884.38 | 226,047.18 |
| 2 months | 405,204.76 | 566,363.76 | 281,628.30 | 540,247.08 |
| 1 Year | 2,431,228.56 | 3,398,182.56 | 1,689,769.80 | 3,241,482.48 |

1.2 Additional Cost for Patients in High Risk Groups

1.2.1 Additional cost of NSAIDs prescriptions compared with specific COX II inhibitors prescriptions for actual practice

Assuming that all high risk patients who were at high risk of upper GI adverse effects.(3) Patients who received NSAIDs at high risk were inappropriate use, they should received specific COX II inhibitors that better than NSAIDs.

For high risk group, total cost of celecoxib use was 77,589.12Baht, total cost of rofecoxib use was 118,956.06 Baht and total cost of NSAIDs use was 26,776.67 Baht in high risk group. Number of high risk of celecoxib use were 81 prescriptions, number of high risk of rofecoxib use were 127 prescriptions and number of high risk of NSAIDS use were 113 prescriptions. Average cost per prescription of celecoxib use was 957.89 Baht, rofecoxib use was 936.66 Baht and NSAIDs use was 236.96 Baht in high risk group (Table 4.8). Average cost per prescription in high risk were calculated as same as in low risk group.

Average cost per day of specific COX II inhibitors and NSAIDs use in high risk group were calculated. Average of duration therapy of receiving celecoxib was 31.17 days, 27.24 days of receiving rofecoxib and 21.13 days of receiving NSAIDs.(Table 4.4). Average cost per day of celecoxib use was 30.73 Baht and average cost per day of rofecoxib use was 34.39 Baht. Average cost per day of NSAIDs use was 11.21 Baht (Table 4.9). Average cost per day of celecoxib use, rofecoxib use and NSAIDS use in high risk group were calculated as same as in low risk group.

The cost difference per day between celecoxib and NSAIDs was 19.52 Baht. The cost difference per day between rofecoxib and NSAIDs was 23.18 Baht. Therefore, the total difference in costs per day in 113 patients of receiving NSAIDs in high risk group compared with celecoxib was 2,205.76 Baht, compared with rofecoxib was 2,619.34 Baht. Average duration therapy of receiving NSAIDs was 21.36 days (Table 4.4). Total additional cost equals the difference cost per day multiplied by average duration therapy. Total additional cost of NSAIDs use compared with celecoxib in high

risk group was 47,115.03 Baht in one course therapy, calculated by the following equation:

$$\text{Total Additional Cost}_{\text{Celecoxib}} = (30.73 - 11.21)\text{Baht} * 113 \text{ Patients} * 21.36 \text{ days}$$
$$= 47{,}115.03 \text{ Baht}$$

In the same way, total additional cost of NSAIDs use in high risk group compared with rofecoxib use was 55,949.10 Baht in one cycle therapy, calculated by the following equation:

$$\text{Total Additional Cost}_{\text{Rofecoxib}} = (34.39 - 11.21)\text{ Baht} * 113 \text{ Patients} * 21.36 \text{ days}$$
$$= 55{,}949.10 \text{ Baht}$$

For actual practice, total additional cost NSAIDs in high risk group compared with celecoxib use was 47,115.03 Baht, total additional cost NSAIDs in high risk group compared with rofecoxib use was 55,949.10 Baht.

During two months period, total the 3,229 NSAIDs prescriptions were collected (Figure 4.1). Percentages of high risk per low risk patients of NSAIDs were 19.02 %. The numbers of high risk patients prescribed NSAIDs during two months was 614 patients based on assumption that percentages of high risk per low risk of studying as same as sampling. (Table 4.7)

Difference in cost per day between celecoxib and NSAIDs was 19.52 Baht. The cost difference per day between rofecoxib and NSAIDs was 23.18 Baht. Therefore, the total difference in cost per day in 614 patients of receiving NSAIDs in high risk group compared with celecoxib was 11,985.28 Baht, compared with rofecoxib was 14,232.52 Baht. Average duration that patient of receiving NSAIDs was 21.36 days (Table 4.4). Total additional cost equals the difference cost per day multiplied by average duration. Total additional costs of NSAIDs use compared with celecoxib in high risk group were 256,005.58 Baht in one course therapy, calculated by the following equation:

$$\text{Total Additional Cost}_{\text{Celecoxib}} = (30.73 - 11.21)\text{ Baht} * 614 \text{ Patients} * 21.36 \text{ days}$$
$$= 256{,}005.58 \text{ Baht}$$

In the same manner, total costs of one course NSAIDs therapy compared with rofecoxib therapy in high risk group was 304,006.63 Baht, calculated by the following equation:

$$\text{Total Additional Cost}_{\text{Rofecoxib}} = (34.39\text{-}11.21)\ \text{Baht} * 614\ \text{Patients} * 21.36\ \text{days}$$
$$= 304{,}006.63\ \text{Baht}$$

For two months, total estimated additional cost of NSAIDs use compared with celecoxib use in high risk group was 256,005.58 Baht and total estimated additional cost of NSAIDs use compared with rofecoxib use in high risk group was 304,006.63 Baht.

Total estimated additional cost of NSAIDS use compared with specific COX II inhibitors in one year was calculated by following equation:

$$\text{Total Additional Cost}_{\text{Celecoxib 12 months}} = \text{Total Additional Cost}_{\text{2 months}}\ (\text{Baht}) * 6$$
$$= 256{,}005.58 * 6$$
$$= 1{,}536{,}033.48\ \text{Baht}$$
$$\text{Total Additional Cost}_{\text{Rofecoxib 12 months}} = \text{Total Additional Cost}_{\text{2 months}}\ (\text{Baht}) * 6$$
$$= 304{,}006.63 * 6$$
$$= 1{,}824{,}039.78\ \text{Baht}$$

For one year, total estimated additional cost of NSAIDs use compared with celecoxib use in high risk group was 1,536,033.48 Baht and total estimated additional cost of NSAIDs use compared with rofecoxib use in high risk group was 1,824,039.78 Baht. The result of total additional cost of NSAIDs compared with specific COX II inhibitors in high risk group for actual practice was displayed in Table 4.18.

Table 4.18: Total Additional Cost of NSAIDs compared with Specific COX II Inhibitors in High Risk Patients.

| | NSAIDs | | Celecoxib | | | Rofecoxib | | |
|---|---|---|---|---|---|---|---|---|
| Actual Practice | N | Average Duration (Days) | No. of High Risk equal NSAIDs | Difference Cost per day (Baht)* | Total Cost (Baht) | No. of High Risk equal NSAIDs | Difference Cost per day (Baht)* | Total Cost (Baht) |
| Sample | 594 | 21.36 | 113 | 19.52 | 47,115.03 | 113 | 23.18 | 55,949.10 |
| 2 months | 3,229 | 21.36 | 614 | 19.52 | 256,005.58 | 614 | 23.18 | 304,006.63 |
| 1 Year | | | | | 1,536,033.48 | | | 1,824,039.78 |

Note: * Difference Cost per Day of Specific COX II inhibitors Compared With NSAIDs Use in High Risk Group.
; cost per day $_{Celecoxib}$ = 30.73 Baht
cost per day $_{Rofecoxib}$ = 34.39 Baht
cost per day $_{NSAIDs}$ = 11.21 Baht