

Drug Class Review on Cyclo-oxygenase (COX)-2 Inhibitors and Non-steroidal Anti-inflammatory Drugs (NSAIDs)



Update #4: Preliminary Scan Report #2

September 2008

The purpose of this report is to make available information regarding the comparative effectiveness and safety profiles of different drugs within pharmaceutical classes. Reports are not usage guidelines, nor should they be read as an endorsement of, or recommendation for, any particular drug, use or approach. Oregon Health & Science University does not recommend or endorse any guideline or recommendation developed by users of these reports.

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OBJECTIVE:

The purpose of this preliminary updated literature scan process is to provide the Participating Organizations with a preview of the volume and nature of new research that has emerged subsequent to the previous full review process. Provision of the new research presented in this report is meant only to assist with Participating Organizations' consideration of allocating resources toward a full update of this topic. Comprehensive review, quality assessment and synthesis of evidence from the full publications of the new research presented in this report would follow only under the condition that the Participating Organizations ruled in favor of a full update. The literature search for this report focuses only on new randomized controlled trials, and actions taken by the FDA or Health Canada since the last report. Other important studies could exist.

Date of Last Update:

Final Report Update #3 November 2006 (searches from 1966 to February Week 2 2006). The first preliminary update scan for consideration of Update #4 was performed in October of 2007.

Scope and Key Questions

The purpose of this review is to compare the benefits and harms of different pharmacologic treatments for beta2-agonists. The Oregon Evidence-based Practice Center wrote preliminary key questions, identifying the populations, interventions, and outcomes of interest, and based on these, the eligibility criteria for studies. These were reviewed and revised by representatives of organizations participating in the Drug Effectiveness Review Project (DERP). The participating organizations of DERP are responsible for ensuring that the scope of the review reflects the populations, drugs, and outcome measures of interest to both clinicians and patients. The participating organizations approved the following key questions to guide this review:

Scope and Key Questions

1. Are there differences in effectiveness between coxibs and other NSAIDs?
2. Are there clinically important differences in short-term safety or adverse effects between coxibs, other NSAIDs, and the combination of an NSAID plus antiulcer medication when used for musculoskeletal pain?
3. Are there clinically important differences in long-term safety or adverse effects between coxibs, other NSAIDs, and the combination of an NSAID plus antiulcer medication when used chronically?
4. Are there subgroups of patients based on demographics, other medications (e.g., aspirin), or co-morbidities for which one medication is more effective or associated with fewer adverse effects?

Several aspects of the key questions merit comment:

1. *Patients.* We focused on patients with chronic pain from osteoarthritis, rheumatoid arthritis, soft-tissue pain, or back pain. We included ankylosing spondylitis. COX-2 inhibitors are also used to treat dysmenorrhea and acute

pain (e.g., dental or surgical pain), and to prevent the formation of colorectal polyps. We did not examine studies of the use of coxibs for these indications.

2. *Efficacy*. The main efficacy measures are pain, functional status, and discontinuations due to lack of efficacy. Measures vary among studies.

Frequently used measures are:

Visual analogue scale (VAS): The patient indicates their level of pain, function, or other outcome by making a mark on a scale labeled with numbers (such as 0 to 100) or descriptions (such as “none” to “worst pain I’ve ever had”).

The *Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC)* is a 24-item questionnaire used to assess the functional status of patients with osteoarthritis of the knee and hip. A lower score indicates better function.

Patient Global Assessment of Disease Status and *Investigator Global Assessment of Disease Status*. The patient or investigator answers questions about the overall response to treatment, functional status, and pain response, using a VAS or Likert scale.

American College of Rheumatology (ACR) criteria measure disease activity and response to treatment. ACR 20, ACR 50, or ACR 70 reflect either an improvement to the 20%, 50%, or 70% level in the parameters outlined.

3. *Safety and adverse effects*. The following events were included in the review:

- a. Serious GI events (GI bleeding, symptomatic ulcer disease, perforation of the GI tract, and death).
- b. Serious cardiovascular events (myocardial infarction, angina, stroke, transient ischemic attack, cardiovascular death, and related measures).
- c. Tolerability and adverse events. We recorded discontinuation due to any adverse event, any serious adverse event, the overall rate of adverse events, the rate of GI adverse events, and the combined rate of adverse events related to renal and cardiovascular function, including increased creatinine, edema, hypertension, or congestive heart failure. We also recorded the frequency of, and discontinuations due to, abnormal laboratory tests, primarily elevated transaminases (liver tests).

Several types of adverse events were excluded:

- d. The main non-clinical, or intermediate, outcome measure for GI adverse effect is *endoscopic ulcer*. Ulcers in the stomach or small intestine can be seen in up to 40% of patients taking NSAIDs. (Hawkey, Laine et al. 2000; Laine, Maller et al. 2004) Up to 85% of these ulcers can only be found by endoscopy because they do not cause symptoms or bleeding. All three COX-2 inhibitors in the US market significantly reduce the incidence of these asymptomatic ulcers. Based on input from the subcommittee, we did not include endoscopic ulcer as an outcome measure, since our focus is on clinically significant adverse events.
- e. *Case reports associated with celecoxib*: anaphylaxis, (Grob, Pichler et al. 2002) fatal (Schneider, Meziani et al. 2002) and nonfatal allergic vasculitis, (Gscheidel, Daspert et al. 2002; Jordan, Edwards et al. 2002) interstitial nephritis with (Alper, Meleg-Smith et al. 2002) and without (Henao, Hisamuddin et al. 2002) nephritic syndrome, cholestatic hepatitis, (Alegria, Lebre et al. 2002) toxic epidermal necrolysis, (Berger, Dwyer et al. 2002;

Friedman, Orlet et al. 2002; Verbeiren, Morant et al. 2002; Giglio 2003) erythema multiforme,(Ernst and Egge 2002) migratory pulmonary infiltrates,(Mehandru, Smith et al. 2002) acute pancreatitis,(Nind and Selby 2002) torsade de pointes,(Pathak, Boveda et al. 2002) and renal papillary necrosis.(Akhund, Quinet et al. 2003)

4. *Drugs.* We sought evidence about the following NSAIDs currently available in the US or Canada:

Table 1. Included NSAIDs

Generic Name	Proprietary Name	Dosage Forms
CELECOXIB	Celebrex	100, 200, 400 mg
DICLOFENAC SODIUM	Voltaren, Voltaren-XR	25, 50, 75, 100 mg
DICLOFENAC POTASSIUM	Cataflam	25, 50 mg
DIFLUNISAL	Dolobid	250, 500 mg
ETODOLAC	Lodine, Lodine XL	200, 300, 400, 500 mg
FENOPROFEN	Nalfon	200, 300, 600 mg
FLURBIPROFEN	Ansaid	50, 100 mg
IBUPROFEN	Motrin	300, 400, 600, 800 mg
INDOMETHACIN	Indocin, Indocin SR	25, 50, 75 mg
KETOPROFEN		25, 50, 75 mg
KETOPROFEN XR	Oruvail	100, 150, 200 mg
KETOROLAC	Toradol	10 mg
MECLOFENAMATE		50, 100 mg
MEFENAMIC ACID		250 mg
MELOXICAM	Mobic	7.5, 15 mg
NABUMETONE	Relafen	500, 750 mg
NAPROXEN		250, 375, 500 mg
NAPROXEN delayed release		375, 500 mg
NAPROXEN SODIUM	Anaprox, Anaprox DS	250, 500 mg
OXAPROZIN	Naprelan	375, 500, 750 mg
PIROXICAM	Daypro	600 mg
PIROXICAM	Feldene	10, 20 mg
SALSALATE	Disalcid	100, 500 mg
SULINDAC	Clinoril	150, 200 mg
TIAPROFENIC ACID	Surgam	200, 300, 600 mg
TENOXICAM	Mobiflex	20, 40 mg
TOLMETIN	Tolectin	200, 400, 600 mg

METHODS

Literature Search

To identify relevant citations for this scan update, we searched MEDLINE (September week 2 2007 to September week 1 2008). We used terms for included drugs and limits for humans, English and randomized clinical trials or controlled clinical trials. We also searched the FDA (<http://www.fda.gov/cder/Offices/DDI/pathfinder.htm>) and Health Canada (http://www.hc-sc.gc.ca/dhp-mps/medeff/advisories-avis/prof/2007/index_e.html) websites for identification of

new drugs, indications, and safety alerts. All citations were imported into an electronic database (EndNote 9.0).

Study Selection

One reviewer assessed abstracts of citations identified from literature searches for inclusion, using the criteria described above.

RESULTS

Overview

We identified 267 potentially relevant citations. Of those, we identified only 3 new potentially relevant controlled clinical trials (Appendix A). Table 2 provides details regarding the treatment comparisons and populations addressed in these trials. Taken together with the 2 new trials identified in the first preliminary update literature scan (Appendix B), now there are a total of 5 trials likely to be added in a full update of this topic.

Table 2. New potentially relevant trials

Author Year	Treatment comparisons	Population
Goldstein 2007	Celecoxib+aspirin vs naproxen+lansoprazole+aspirin	Osteoarthritis: focus on GI safety
Sieper 2008	Celecoxib vs diclofenac	Ankylosing spondylitis
Wagenitz 2007	Comparison of two sustained-release forms of diclofenac	Osteoarthritis

New FDA-approved Drugs

None

Potential New Drugs

We are aware of at least one new COX-2 inhibitor, GW406381, in development by GSK. As part of this scan, we identified one new published clinical trial of a single-dose as used to treat acute migraine. However, as acute migraine is not an included population in this review, we did not list the abstract of that publication in this report. A search of clinicaltrials.gov also identified listings for two additional completed Phase III trials in adults with rheumatoid arthritis and osteoarthritis, respectively (Appendix C). But we did not find publications of these in our Medline searches. We were unable to identify any further information about if and when FDA-approval of this compound is anticipated.

New Indications

None

New Safety Alerts

None

Other considerations

Previously the focus of this review has been limited to usage of oral formulations for treatment of chronic pain from osteoarthritis, rheumatoid arthritis, soft-tissue or back pain, or ankylosing spondylitis. However, in the event of a full update, interest has been expressed in expanding the scope to include available topical agents. Below is a preliminary list of the known topical NSAID products:

Diclofenac 1% topical gel (Voltaren®) – FDA-approved on 10/17/07

Diclofenac 1.3% topical patch (Flector®) – FDA-approved on 1/31/07

Diclofenac 3% topical gel (Solaraze®) – FDA-approved in 2000

In order to estimate the size of the increase in the volume of the body of evidence that may be associated with such a scope expansion, we also looked for trials of topical agents in this scan, as well as re-reviewed results of the previous scan. We only found two relevant trials, both involving diclofenac gel. Abstracts of those are included in Appendix A and some brief details are listed in Table 3. We also note that the September 2006 AHRQ Effective Healthcare ‘Comparative Effectiveness and Safety of Analgesics for Osteoarthritis’ included an evaluation of trials that compared topical and oral NSAIDs.

Table 3. New trials of topical diclofenac

Author Year	Treatment comparisons	Population
D’Anchise 2007	Diclofenac gel vs comfrey extract	Acute pain
Esparza 2007	Diclofenac gel vs topical ketoprofen TDS patch	Sport related soft-tissue injury

APPENDIX A

D'Anchise, R., M. Bulitta, et al. (2007). "Comfrey extract ointment in comparison to diclofenac gel in the treatment of acute unilateral ankle sprains (distortions)." Arzneimittel-Forschung **57**(11): 712-6.

Objectives: A previously published study comparing the efficacy of comfrey extract to a commercial diclofenac (CAS 78213-16-8) preparation in the treatment of unilateral ankle sprains is critically re-evaluated. The study was designed to show non-inferiority of the comfrey extract. The data were re-evaluated for superiority according to CPMP guidelines. The study was an observer-blind, randomised, multi-centre clinical trial with two independent treatment groups "comfrey extract" and "diclofenac gel" (parallel group design) and included a total of 164 patients (82 in the comfrey group and 82 in the diclofenac group, intention-to-treat (ITT) analysis). Key variables were the area under the curve (AUC) from Visits 1 to 2 of the difference of the tenderness values contra-lateral minus injured side (primary variable), pain assessment (Visual Analogue Scale, VAS) at rest and on movement by patient, swelling (figure-of-eight method) and ankle movement (neutral zero method). On average (mean difference comfrey extract minus diclofenac), the AUC was +61.1 h x N/cm² greater for patients treated with comfrey extract compared to diclofenac treated patients (95% confidence interval: 19.08; 103.09 h x N/cm²). The difference between the two treatment groups was statistically significant (analysis of variance with factors "study drug", "centre", and "drug x centre interaction"). Safety was excellent in both treatment groups. The re-evaluation of the data showed superiority of the plant based ointment over the diclofenac gel in the treatment of distortions. It is encouraging and impressive to realize that a natural product seems to be an effective and safe alternative to the standard topical treatment with diclofenac.

Esparza, F., C. Cobian, et al. (2007). "Topical ketoprofen TDS patch versus diclofenac gel: efficacy and tolerability in benign sport related soft-tissue injuries." British Journal of Sports Medicine **41**(3): 134-9.

OBJECTIVE: To compare the ketoprofen TDS patch with diclofenac gel in the treatment of traumatic acute pain in benign sport-related soft-tissue injuries. DESIGN: 7-14 treatment days, prospective, randomised, open study. PATIENTS: Outpatients aged 18-70 years diagnosed for painful benign sport-related soft-tissue injury (sprains, strains and contusions within the prior 48 h), randomised to either ketoprofen patch 100 mg once daily (n = 114) or diclofenac gel 2-4 g three times daily (n = 109). INTERVENTION: 7-14 days of topical non-steroidal anti-inflammatory drugs treatment to assess the pain intensity changes (daily activities and spontaneous at rest) in a daily diary (100-mm Visual Analogue Scale (VAS)). Main outcome measurement: Pain intensity (VAS). RESULTS: The ketoprofen patch was not inferior to diclofenac gel in reducing the baseline pain during daily activities (difference of -1.17 mm in favour of ketoprofen patch, 95% CI (-5.86 to 3.52), reducing to the baseline VAS 79%. Ketoprofen patch presented also a higher cure rate (64%) than diclofenac gel (46%) at day 7 (p = 0.004).

Patient opinions about the treatment comfort (pharmaceutical shape, application and dosage) were also statistically higher for the ketoprofen patch (>80% of the patients rated as good or excellent the patch removal and skin adherence). CONCLUSION: Ketoprofen patches are effective and safe pain relievers for the treatment of sports injury pain with advantages compared with diclofenac gel.

Goldstein, J. L., B. Cryer, et al. (2007). "Celecoxib plus aspirin versus naproxen and lansoprazole plus aspirin: a randomized, double-blind, endoscopic trial." Clinical Gastroenterology & Hepatology 5(10): 1167-74.

BACKGROUND & AIMS: Patients requiring low-dose aspirin along with nonsteroidal anti-inflammatory drugs are at increased risk for gastrointestinal injury. This study compared the incidence of gastroduodenal ulcers in patients treated with low-dose aspirin and a cyclooxygenase-2 selective nonsteroidal anti-inflammatory drug or a nonselective nonsteroidal anti-inflammatory drug plus the proton pump inhibitor lansoprazole. METHODS: Subjects 18 years or older with osteoarthritis, without gastroduodenal ulcer or erosive esophagitis at baseline endoscopy, and a cardiovascular indication for prophylaxis low-dose (81 or 325 mg) aspirin were prescribed open-label aspirin and blindly randomized to celecoxib 200 mg/day or naproxen 500 mg twice daily plus lansoprazole 30 mg once daily. Endoscopy was performed at 12 weeks or early termination. RESULTS: One thousand forty-five subjects were randomized and received at least 1 dose of study medication, and 854 (n = 426 celecoxib, n = 428 naproxen plus lansoprazole) subjects with both baseline and final visit endoscopies were evaluable for the primary efficacy analysis. Among these subjects, the rate of endoscopically confirmed gastroduodenal ulcers was not different in the celecoxib (9.9%) and naproxen plus lansoprazole (8.9%; treatment difference [95% confidence interval], 1.0% [-2.9% to 4.9%]) groups. CONCLUSIONS: In patients with osteoarthritis taking low-dose aspirin, the use of celecoxib or naproxen plus lansoprazole resulted in similar rates of gastroduodenal ulceration.

Sieper, J., T. Klopsch, et al. (2008). "Comparison of two different dosages of celecoxib with diclofenac for the treatment of active ankylosing spondylitis: results of a 12-week randomised, double-blind, controlled study." Annals of the Rheumatic Diseases 67(3): 323-9.

OBJECTIVES: To demonstrate the non-inferiority of celecoxib compared with diclofenac in subjects with ankylosing spondylitis (AS). METHODS: The basis of the present work was a 12-week randomised, double-blind, controlled study in active AS subjects with three treatment arms: celecoxib 200 mg once a day, celecoxib 200 mg twice a day, and diclofenac SR 75 mg twice a day. The primary efficacy endpoint was the change from baseline in global pain intensity on a visual analogue scale (VAS) at week 12. Secondary endpoints covered changes in disease activity, functional and mobility capacities, and adverse events. RESULTS: A total of 458 subjects were randomly assigned to either celecoxib 200 mg once a day (n = 153), celecoxib 200 mg twice a day (n = 150), or diclofenac (n = 155). Least square (LS) mean changes from baseline at week 12 on a pain VAS were clinically relevant in all treatment groups (celecoxib 200 mg once a day: -29.1 mm; celecoxib 200 mg twice a day: -31.7 mm; diclofenac: -32.7 mm) and non-inferior

when compared to diclofenac. Ankylosing Spondylitis Assessment Study group 20% (ASAS 20) response and mean improvement in Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) scores at week 12 were numerically better on celecoxib 200 mg twice a day (59.7% and -1.32 points) and on diclofenac (60.2% and -1.48 points) than on celecoxib 200 mg once a day (46.0% and -0.99 points). The incidence of gastrointestinal adverse events was significantly higher on diclofenac (28.4%) than on celecoxib 200 mg once a day (15.0%) or 200 mg twice a day (16.7%). CONCLUSIONS: The efficacy of celecoxib 200 mg once a day and 200 mg twice a day was comparable to that of diclofenac 75 mg twice a day with respect to pain reduction. Celecoxib 200 mg twice a day and diclofenac reduced some parameters associated with inflammation more effectively than celecoxib 200 mg once a day. Treatment was well tolerated, with celecoxib (either dose) exhibiting less frequent gastrointestinal adverse events than diclofenac.

Wagenitz, A., E. A. Mueller, et al. (2007). "Comparative efficacy and tolerability of two sustained-release formulations of diclofenac: results of a double-blind, randomised study in patients with osteoarthritis and a reappraisal of diclofenac's use in this patient population." Current Medical Research & Opinion **23**(8): 1957-66.

OBJECTIVE: To compare the analgesic efficacy and tolerability of a sustained-release pellet formulation of diclofenac (Olfen-100 SR Depocaps, SR-CAP, Mepha Ltd, Aesch, Switzerland) with the standard reference formulation (Voltaren retard 100, SR-TAB, Novartis Pharma AG, Basel, Switzerland), both containing 100 mg diclofenac sodium, in patients with osteoarthritis (OA) of the knee and/or hip. In addition, diclofenac's current place in the symptomatic therapy of OA is briefly reviewed. METHODS: In this 2-week double-blind, active-controlled, non-inferiority trial, 210 OA patients were randomised to receive either SR-CAP once daily or SR-TAB once daily (n = 105 for both groups). The primary efficacy endpoint was the change in visual analogue scale (VAS) pain score (0-100 mm) at rest at Day 14 compared with baseline. Secondary variables included the change in VAS pain score on movement and global assessments of efficacy and tolerability using verbal rating scales (VRS). RESULTS: Between baseline and Day 14, mean +/- SD VAS pain score at rest decreased by 44.4 +/- 18.5 mm in the SR-CAP group (n = 89) compared with 41.2 +/- 19.8 mm in the SR-TAB group (n = 82) based on the per protocol population. Comparable changes were observed in the intention-to-treat population. The lower bound of the 1-sided 97.5% confidence interval was -2.7 mm and greater than the prespecified non-inferiority limit of -10 mm. There was a trend towards a better tolerability with SR-CAP compared with SR-TAB based on mean +/- SD VRS scores (SR-CAP, 0.6 +/- 0.68; SR-TAB, 0.9 +/- 1.0 for assessment by patients; p = 0.063). CONCLUSION: SR-CAP is as effective as and possibly better tolerated than SR-TAB in patients suffering from painful OA.

Appendix B. New Trials Identified in Preliminary Update Scan #1

Pincus, T., X. Wang, et al. (2005). "Patient preference in a crossover clinical trial of patients with osteoarthritis of the knee or hip: face validity of self-report questionnaire ratings.[erratum appears in J Rheumatol. 2005 May;32(5):966]." Journal of Rheumatology **32**(3): 533-9.

OBJECTIVE: To analyze correlational validity of self-report responses regarding patient preference between 2 drugs at the conclusion of a crossover double-blind clinical trial in patients with osteoarthritis (OA) of the knee or hip. **METHODS:** Patients were randomized to 6 weeks' treatment of diclofenac/misoprostol or acetaminophen, followed by crossover to 6 weeks of the other drug. Patient preference was queried at the final visit: "Please compare control of your arthritis during the first and second periods as 'much better' or 'better' in the first period, 'no different' or 'better' or 'much better' in the second period." Patient preference ratings were evaluated in comparisons with 4 independent self-report measures within each treatment period: (1) change in Western Ontario McMaster (WOMAC) questionnaire scores; (2) change in pain visual analog scale (VAS) on a multidimensional Health Assessment Questionnaire (MDHAQ); (3) patient ratings of drug efficacy; and (4) patient report of change in arthritis status, as well as investigator ratings of the more efficacious drug. **RESULTS:** Among 173 patients, diclofenac/misoprostol was rated as "much better" by 54 and "better" by 45, acetaminophen was rated as "better" by 18 and "much better" by 17, and "no difference" by 39 patients. Spearman rank correlations for patient preferences were significant for changes in WOMAC scores, pain VAS, and independent patient ratings of drug efficacy and changes in arthritis status within each treatment period, as well as with physician ratings of the more efficacious drug ($p < 0.001$). **CONCLUSION:** Significant correlational validity is documented for patient self-report of preferences between 2 drugs compared to independent measures within each treatment period in this crossover clinical trial in patients with OA of the knee or hip.

Soininen, H., C. West, et al. (2007). "Long-term efficacy and safety of celecoxib in Alzheimer's disease." Dementia & Geriatric Cognitive Disorders **23**(1): 8-21.

BACKGROUND/AIMS: Cyclooxygenase-2 (COX-2) may play an important role in the neuropathology of Alzheimer's disease (AD). The efficacy and safety of celecoxib (200 mg bid), a COX-2 selective inhibitor, were assessed in patients $> \text{ or } = 50$ years with established mild-to-moderate AD to determine whether treatment was effective in retarding deterioration of cognitive function. **METHODS:** This was a 52-week, multicenter, randomized, double-blind, placebo-controlled, parallel-group study. The primary efficacy end points were the change from baseline to week 52 in the Alzheimer's Disease Assessment Scale-Cognitive Behavior (ADAS-cog) composite score and the week 52 Clinician's Interview-Based Impression of Change Plus (CIBIC+). **RESULTS:** At 52 weeks, change in ADAS-cog scores from baseline was similar for placebo and celecoxib 200 mg bid groups (5.00 and 4.39, respectively). CIBIC+ scores were also similar (4.83 and 4.92). Two extension studies were conducted but were terminated early based on these efficacy results. Safety data from all 3 studies indicated that celecoxib was generally well-tolerated. **CONCLUSION:** Celecoxib 200 mg bid did not slow the progression of AD in this study, and the occurrence of adverse events was as expected for an elderly population with a complex chronic medical condition. Copyright 2007 S. Karger AG, Basel

Appendix C. Clinicaltrials.gov listings of relevant trials of investigational COX-2 inhibitor in development by GSK

COX-2 Inhibitor Study In Patients With Rheumatoid Arthritis

This study has been completed.

Sponsored by:	GlaxoSmithKline
Information provided by:	GlaxoSmithKline
ClinicalTrials.gov Identifier:	NCT00113308

 Purpose

This study is being conducted to find out if an investigational drug called GW406381 can help people with rheumatoid arthritis.

<u>Condition</u>	<u>Intervention</u>	<u>Phase</u>
Rheumatoid Arthritis	Drug: GW406381	Phase III

[MedlinePlus](#) related topics: [Rheumatoid Arthritis](#)

[U.S. FDA Resources](#)

Study Type: Interventional

Study Design: Treatment, Randomized, Double-Blind, Placebo Control, Single Group Assignment, Safety/Efficacy Study

Official Title: A Phase III, 12-Week, Multicentre, Double-Blind, Randomised, Placebo- and Active Comparator-Controlled, Parallel Group Study to Investigate the Efficacy and Safety of GW406381, 5mg, 10mg, 25mg, and 50mg Administered Orally Once Daily, in Adults With Rheumatoid Arthritis

Further study details as provided by GlaxoSmithKline:


Primary Outcome Measures:

- 20% improvement in the number of tender/painful joints & swollen joints, 20% improvement in at least 3 of the following: patient's pain, patient's or physician's global impression of arthritis, functional disability, and c-reactive protein.

Secondary Outcome Measures:

- Change in the individual components of ACR20 as listed above at each scheduled visit. Subjects discontinuing due to lack of efficacy, use of rescue medication, adverse events, safety measures (labs, ECG, vital signs) and health-related quality of life.

Enrollment: 2208
Study Start Date: June 2005

 Eligibility

Ages Eligible for Study: 18 Years and older
Genders Eligible for Study: Both
Accepts Healthy Volunteers: No

Criteria

Inclusion criteria:

- Rheumatoid arthritis (RA) for at least 12 months.
- Required a non-steroidal anti-inflammatory drug (NSAID) or COX-2 inhibitor for RA for at least 5 out of 7 days of each week for the 4 weeks prior to screening.

Exclusion criteria:

- Any history of cardiovascular disease (e.g., heart attack, stroke, congestive heart failure, uncontrolled high blood pressure), documented peripheral arterial insufficiency and symptomatic, clinically significant claudication, or who have a history of peripheral arterial embolism.
- Have an active stomach ulcer or history of any stomach tear or bleeding.

 Contacts and Locations

Please refer to this study by its ClinicalTrials.gov identifier: NCT00113308

 [Show 437 Study Locations](#)

Sponsors and Collaborators
GlaxoSmithKline

Investigators

Study Director: GSK Clinical Trials, MD GlaxoSmithKline

 More Information

Study ID Numbers: CXA30009

First Received: June 7, 2005
 Last Updated: August 22, 2007
 ClinicalTrials.gov Identifier: [NCT00113308](#)
 Health Authority: United States: Food and Drug Administration

Keywords provided by GlaxoSmithKline:
 Rheumatoid Arthritis
 COX-2 Inhibitor

Study placed in the following topic categories:
 Autoimmune Diseases Connective Tissue Diseases
 Musculoskeletal Diseases Arthritis, Rheumatoid
 Joint Diseases Rheumatic Diseases
 Arthritis

Additional relevant MeSH terms:
 Immune System Diseases

ClinicalTrials.gov processed this record on September 17, 2008

Evaluation of GW406381 in Treating Adults With Osteoarthritis Of The Knee

This study has been completed.

Sponsored by:	GlaxoSmithKline
Information provided by:	GlaxoSmithKline
ClinicalTrials.gov Identifier:	NCT00120900

 Purpose

This study was designed to evaluate the effectiveness of GW406381 (a COX-2 inhibitor) in treating the signs and symptoms of osteoarthritis of the knee.

Condition	Intervention	Phase
Osteoarthritis of the Knee	Drug: GW406381	Phase III

[MedlinePlus](#) related topics: [Osteoarthritis](#)

[U.S. FDA Resources](#)

Study Type: Interventional
Study Design: Treatment, Randomized, Double-Blind, Placebo Control, Parallel Assignment, Safety/Efficacy Study
Official Title: A Phase III, 12-Week, Multicentre, Double-Blind, Double-Dummy, Randomised, Placebo- and Active Comparator-Controlled, Parallel Group Study to Investigate the Efficacy and Safety of GW406381 1mg, 5mg, 10mg, 25mg and 50mg Administered Orally Once Daily, in Adults With Osteoarthritis of the Knee (CXA30007).

Further study details as provided by GlaxoSmithKline:

Primary Outcome Measures:

- Change in OA symptoms at week 12 as measured by scores on subject-completed questionnaires on pain, daily activities and global assessment

Secondary Outcome Measures:

- Change in OA symptoms as measured by subject and physician-completed questionnaires at each scheduled visit. Percentage of responders, subjects discontinuing due to lack of efficacy, use of rescue medication and health-related quality of life.

Estimated Enrollment: 1113

Study Start Date: May 2005

Eligibility

Ages Eligible for Study: 40 Years and older

Genders Eligible for Study: Both

Accepts Healthy Volunteers: No

Criteria


Inclusion criteria:

- Subjects have a primary diagnosis of osteoarthritis of the knee with symptom duration of at least 3 months.
- Use pain medication, such as a COX-2 inhibitor or NSAID (non-steroidal anti-inflammatory drug) at least 5 days per week.

Exclusion criteria:

- History of hypersensitivity or intolerance to pain medications.
- History of gastroduodenal perforations and/or obstructions.
- History of upper GI (gastrointestinal) ulceration within the previous 6 months.
- History of upper or lower GI bleeding within the previous year.

- History of inflammatory bowel disease.
- Currently take sucralfate or misoprostol.
- Currently taking aspirin daily for the heart.
- Other restrictions around the use medications apply and would need to be discussed.
- History of coronary artery disease, (angina, MI) or surgery.
- History of congestive heart failure or renal artery stenosis.
- History of stroke or transient ischemic attack.
- History of uncontrolled hypertension.

 **Contacts and Locations**

Please refer to this study by its ClinicalTrials.gov identifier: NCT00120900


 [Show 270 Study Locations](#)

Sponsors and Collaborators

GlaxoSmithKline

Investigators

Study Director: GSK Clinical Trials, MD GlaxoSmithKline

 **More Information**

Study ID Numbers: CXA30007
First Received: June 30, 2005
Last Updated: September 18, 2006
ClinicalTrials.gov Identifier: [NCT00120900](#)
Health Authority: United States: Food and Drug Administration

Keywords provided by GlaxoSmithKline:

Knee osteoarthritis
COX-2 inhibitor

Study placed in the following topic categories:

Osteoarthritis, Knee	Joint Diseases
Musculoskeletal Diseases	Arthritis
Osteoarthritis	Rheumatic Diseases

ClinicalTrials.gov processed this record on September 17, 2008