LOCAL PRODUCT CIRCULAR

Tablets

ARCOXIA™ (etoricoxib)

Cardiovascular Risk

- NSAIDs may cause an increased risk of serious cardiovascular thrombotic events, myocardial infarction, and stroke, which can be fatal. This risk may increase with duration of use. Elderly patients and patients with cardiovascular disease or risk factors for cardiovascular disease may be at greater risk. (See **WARNINGS)**.

- ARCOXIA is contraindicated for the treatment of peri-operative pain in the setting of coronary artery bypass graft (CABG) surgery (see **WARNINGS**).

Gastrointestinal Risk

- NSAIDs cause an increased risk of serious gastrointestinal adverse events including bleeding, ulceration, and perforation of the stomach or intestines, which can be fatal. These events can occur at any time during use and without warning symptoms. Elderly patients are at greater risk for serious gastrointestinal events. (See **WARNINGS**).

Asthma and Skin Reaction

Arcoxia is contraindicated to patients who have experienced asthma, urticaria, or allergic-type reactions after taking aspirin or other NSAID (**See PRECAUTIONS**).

Congestive Heart Failure and Edema

ARCOXIA should be used with caution in patients with fluid retention or heart failure (see **WARNINGS**)

Hepatic effects

A patients with symptoms and /or signs suggesting liver dysfunction, or in whom an abnormal liver test has occurred, should be evaluated for evidence of the development of a more severe hepatic reaction while on therapy with ARCOXIA (see **PRECAUTIONS**).

Renal Effects

Long-term administration of NSAIDs has resulted in renal papillary necrosis and other renal injury. Renal toxicity has also been seen in patients in whom renal prostaglandins have a compensatory role in the maintenance of renal perfusion (see **PRECAUTIONS**)

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THERAPEUTIC CLASS

ARCOXIA* (etoricoxib) is a member of a class of arthritis/analgesia medications called Coxibs. ARCOXIA is a highly selective inhibitor of cyclooxygenase-2 (COX-2).

COMPOSITION

Each film coated tablet contains etoricoxib 60 mg (ARCOXIA 60), 90 mg (ARCOXIA 90) and 120 mg (ARCOXIA 120).

INDICATIONS

ARCOXIA is indicated for:

- Symptomatic relief in the treatment of osteoarthritis (OA) and rheumatoid arthritis (RA)
- Symptomatic relief in the treatment of ankylosing spondylitis (AS)
- Treatment of pain and signs of inflammation associated with acute gouty arthritis. ARCOXIA should be used only for the acute symptomatic period limited to a maximum of 8 days.
- Relief of chronic musculo-skeletal pain
- Relief of acute pain associated with dental surgery

The decision to prescribe a selective COX-2 inhibitor should be based on an assessment of the individual patient's overall risks (see PRECAUTIONS).

DOSAGE AND ADMINISTRATION

ARCOXIA is administered orally. ARCOXIA may be taken with or without food. ARCOXIA should be administered for the shortest duration possible and the lowest effective daily dose should be used.

Osteoarthritis

The recommended dose is 60 mg once daily.

Rheumatoid Arthritis

The recommended dose is 60 mg once daily. In some patients with insufficient relief from symptoms, an increased dose of 90 mg once daily may increase efficacy.

Ankylosing Spondylitis

The recommended dose is 60 mg once daily. In some patients with insufficient relief from symptoms, an increased dose of 90 mg once daily may increase efficacy.

Chronic Musculoskeletal Pain

The recommended dose is 60 mg once daily.

Acute Gouty Arthritis

The recommended dose is 120 mg once daily. ARCOXIA should be used only for the acute symptomatic period limited to a maximum of 8 days.

Post-operative Dental Pain

The recommended dose is 90 mg once daily.

Doses greater than the maximum recommended for each indication have either not demonstrated additional efficacy or have not been studied. Therefore, the higher dose for each indication is the maximum recommended dose for that indication.

The dose for osteoarthritis should not exceed 60 mg daily.
The dose for rheumatoid arthritis should not exceed 90 mg daily.
The dose for ankylosing spondylitis should not exceed 90 mg daily.
The dose for chronic pain should not exceed 60 mg daily.
The dose for acute gout should not exceed 120 mg daily, limited to a maximum of 8 days treatment.
The dose for post-operative acute dental surgery pain should not exceed 90 mg daily.

Elderly, Gender, Race

No dosage adjustment in ARCOXIA is necessary for the elderly or based on gender or race.

Hepatic Insufficiency

In patients with mild hepatic insufficiency (Child-Pugh score 5-6), a dose of 60 mg once

daily should not be exceeded. In patients with moderate hepatic insufficiency (Child-Pugh score 7-9), the dose should be reduced; a dose of 60 mg ***every other day*** should not be exceeded. There are no clinical or pharmacokinetic data in patients with severe hepatic insufficiency (Child-Pugh score >9). (See PRECAUTIONS.)

Renal Insufficiency

In patients with advanced renal disease (creatinine clearance <30 mL/min), treatment with ARCOXIA is not recommended. No dosage adjustment is necessary for patients with lesser degrees of renal insufficiency (creatinine clearance ≥ 30 mL/min). (See PRECAUTIONS.).

CONTRAINDICATIONS

ARCOXIA is contraindicated in patients with:

- Hypersensitivity to any component of this product.
- Congestive heart failure (NYHA II-IV).
- Established ischemic heart disease, peripheral arterial disease and/or cerebrovascular disease (including patients who have recently undergone coronary artery bypass graft surgery or angioplasty).

WARNINGS

CARDIOVASCULAR EFFECTS

Cardiovascular Thrombotic Events

Clinical trials of several COX-2 selective and nonselective NSAIDs of up to three years duration have shown an increased risk of serious cardiovascular (CV) thrombotic events, myocardial infarction, and stroke, which can be fatal. All NSAIDs, both COX-2 selective and nonselective, may have a similar risk. Patients with known CV disease or risk factors for CV disease may be at greater risk. To minimize the potential risk for an adverse CV event in patients treated with an NSAID, the lowest effective dose should be used for the shortest duration possible. Physicians and patients should remain alert for the development of such events, even in the absence of previous CV symptoms. Patients should be informed about the signs and/or symptoms of serious CV events and the steps to take if they occur.

There is no consistent evidence that concurrent use of aspirin mitigates the increased risk of serious CV thrombotic events associated with NSAID use. The concurrent use of aspirin and an NSAID does increase the risk of serious GI events (see Warnings: Gastrointestinal Effects).

Two large, controlled, clinical trials of a COX-2 selective NSAID for the treatment of pain in the first 10-14 days following CABG surgery found an increased incidence of myocardial infarction and stroke (see Contraindications).

Hypertension

NSAIDs, including ARCOXIA, can lead to onset of new hypertension or worsening of pre-existing hypertension, either of which may contribute to the increased incidence of CV events. Patients taking thiazides or loop diuretics may have impaired response to these therapies when taking NSAIDs. NSAIDs, including ARCOXIA, should be used with caution in patients with hypertension. Blood pressure (BP) should be monitored closely during the initiation of NSAID treatment and throughout the course of therapy.

Congestive Heart Failure and Edema

Fluid retention and edema have been observed in some patients taking NSAIDs. ARCOXIA should be used with caution in patients with fluid retention or heart failure.

Gastrointestinal Effects- Risk of Ulceration, Bleeding, and Perforation

NSAIDs, including ARCOXIA, can cause serious gastrointestinal (GI) adverse events including inflammation, bleeding, ulceration, and perforation of the stomach, small intestine, or large intestine, which can be fatal. These serious adverse events can occur at any time, with or without warning symptoms, in patients treated with NSAIDs. Only one in five patients, who develop a serious upper GI adverse event on NSAID therapy, is symptomatic. Upper GI ulcers, gross bleeding, or perforation caused by NSAIDs occur in approximately 1% of patients treated for 3-6 months, and in about 2-4% of patients treated for one year. These trends continue with longer duration of use, increasing the likelihood of developing a serious GI event at some time during the course of therapy. However, even short-term therapy is not without risk.

NSAIDs should be prescribed with extreme caution in those with a prior history of ulcer disease or gastrointestinal bleeding. Patients with a *prior history of peptic ulcer disease and/or gastrointestinal bleeding* who use NSAIDs have a greater than 10-fold increased risk for developing a GI bleed compared to patients with neither of these risk factors.

Other factors that increase the risk for GI bleeding in patients treated with NSAIDs include concomitant use of oral corticosteroids or anticoagulants, longer duration of NSAID therapy, smoking, use of alcohol, older age, and poor general health status. Most spontaneous reports of fatal GI events are in elderly or debilitated patients and therefore, special care should be taken in treating this population.

To reduce the risk of gastroinstestinal effect on NSAID therapy, the lowest effective dose must be given in short term therapy. Doctor and patient must be caution on sign and symptoms of ulceration and gastrointestinal bleeding during NSAID therapy. If there is serious gastrointestinal effects suspected, evaluate immediately and give additional treatment. For high risk patient, alternative therapy that does not include NSAID can be considered.

PRECAUTIONS

Clinical trial suggest that the selective COX-2 inhibitor class of drugs may be associated with an increased risk of thrombotic events (especially MI and stroke), relative to placebo and some NSAIDs (naproxen). As the cardiovascular risks of selective COX-2 inhibitors may increase with dose and duration of exposure, the shortest duration possible and the lowest effective daily dose should be used. The patients need for symptomatic relief and response to therapy should be re-evaluated periodically.

Patients with significant risk factors for cardiovascular events (e.g. hypertension, hyperlipidaemia, diabetes mellitus, smoking) or peripheral arterial disease should only be treated with etoricoxib after careful consideration.

Selective COX-2 inhibitors are not a substitute for aspirin for cardiovascular prophylaxis because of their lack of effect on platelets. Because etoricoxib, a member of this class, does not inhibit platelet aggregation, antiplatelet therapies should not be discontinued.

There is a further increase in the risk of gastrointestinal adverse effects (gastrointestinal ulceration or other gastrointestinal complications) for etoricoxib, other selective COX-2 inhibitors and NSAIDs, when taken concomitantly with acetylsalicylic acid (even at low doses). The relative differences in gastrointestinal safety between selective COX-2 inhibitors + acetylsalicylic acid vs. NSAIDs + acetylsalicylic acid has not been

adequately evaluated in long term clinical trials.

In patients with advanced renal disease, treatment with ARCOXIA is not recommended. Clinical experience in patients with estimated creatinine clearance of <30 mL/min is very limited. If therapy with ARCOXIA must be initiated in such patients, close monitoring of the patient's renal function is advisable.

Long term administration of NSAIDs has resulted in renal papillary necrosis and other injury. Renal prostaglandins may play a compensatory role in the maintenance of renal perfusion. Therefore, under conditions of compromised renal perfusion, administration of ARCOXIA may cause a reduction in prostaglandin formation and, secondarily, in renal blood flow, and thereby impair renal function. Patients at greatest risk of this response are those with pre-existing significantly impaired renal function, uncompensated heart failure, or cirrhosis. Monitoring of renal function in such patients should be considered.

Caution should be used when initiating treatment with ARCOXIA in patients with considerable dehydration. It is advisable to rehydrate patients prior to starting therapy with ARCOXIA.

As with other drugs known to inhibit prostaglandin synthesis, fluid retention, edema and hypertension have been observed in some patients taking ARCOXIA. The possibility of fluid retention, edema or hypertension should be taken into consideration when ARCOXIA is used in patients with pre-existing edema, hypertension, or heart failure. All Nonsteroidal Antiinflammatory Drugs (NSAIDs), including etoricoxib, can be associated with new onset or recurrent congestive heart failure. (See SIDE EFFECTS.). Etoricoxib may be associated with more frequent and severe hypertension than some other NSAIDs and selective COX-2 inhibitors, particularly at high doses. Therefore, special attention should be paid to blood pressure monitoring during treatment with etoricoxib. If blood pressure rises significantly, alternative treatment should be considered.

Physicians should be aware that individual patients may develop upper gastrointestinal (GI) ulcers/ulcer complications irrespective of treatment. Upper gastrointestinal complications [perforations, ulcers or bleedings (PUBs)], some of them resulting in fatal outcome, have occurred in patients treated with etoricoxib. Caution is advised with

treatment of patients most at risk of developing a gastrointestinal complication with NSAIDs; the elderly, patients using any other NSAID or acetylsalicylic acid concomitantly or patients with a prior history of gastrointestinal disease, such as ulceration and GI bleeding. There is a further increase in the risk of gastrointestinal adverse effects (gastrointestinal ulceration or other gastrointestinal complications) when etoricoxib is taken concomitantly with acetylsalicylic acid (even at low doses). A significant difference in GI safety between selective COX-2 inhibitors + acetylsalicylic acid vs. NSAIDs + acetylsalicylic acid has not been demonstrated in long-term clinical trials.

Elevations of alanine aminotransferase (ALT) and/or aspartate aminotransferase (AST) (approximately three or more times the upper limit of normal) have been reported in approximately 1% of patients in clinical trials treated for up to one year with ARCOXIA 30, 60 and 90 mg daily. In active comparator portions of clinical trials, the incidence of elevated AST and/or ALT in patients treated with ARCOXIA 60 and 90 mg daily was similar to that of patients treated with naproxen 1000 mg daily, but notably less than the incidence in the diclofenac 150 mg daily group. These elevations resolved in patients treated with ARCOXIA, with approximately half resolving while patients remained on therapy. In controlled clinical trials of ARCOXIA 30 mg daily versus ibuprofen 2400 mg daily or celecoxib 200 mg daily, the incidence of elevations of ALT or AST was similar.

A patient with symptoms and/or signs suggesting liver dysfunction, or in whom an abnormal liver function test has occurred, should be evaluated for persistently abnormal liver function tests. If persistently abnormal liver function tests (three times the upper limit of normal) are detected, ARCOXIA should be discontinued.

ARCOXIA should be used with caution in patients who have previously experienced acute asthmatic attacks, urticaria, or rhinitis, which were precipitated by salicylates or non-selective cyclooxygenase inhibitors. Since the pathophysiology of these reactions is unknown, physicians should weigh the potential benefits of prescribing ARCOXIA versus the potential risks.

When using etoricoxib in the elderly and in patients with renal, hepatic, or cardiac dysfunction, medically appropriate supervision should be maintained. If these patients

deteriorate during treatment, appropriate measures should be taken, including discontinuation of therapy.

Serious skin reactions, some of them fatal, including exfoliative dermatitis, Stevens-Johnson syndrome, and toxic epidermal necrolysis, have been reported very rarely in association with the use of NSAIDs and some selective COX-2 inhibitors during post-marketing surveillance (see SIDE EFFECTS). These serious events may occur without warning. Patients appear to be at highest risk for these reactions early in the course of therapy: the onset of the reaction occurring in the majority of cases within the first month of treatment. Serious hypersensitivity reactions (such as anaphylaxis and angioedema) have been reported in patients receiving etoricoxib (see SIDE EFFECTS). Some selective COX-2 inhibitors have been associated with an increased risk of skin reactions in patients with a history of any drug allergy. Etoricoxib should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity.

ARCOXIA may mask fever, which is a sign of infection. The physician should be aware of this when using ARCOXIA in patients being treated for infection.

PREGNANCY

As with other drugs known to inhibit prostaglandin synthesis, use of ARCOXIA should be avoided in late pregnancy because it may cause premature closure of the ductus arteriosus.

Cases of fetal renal dysfunction that have resulted in reduction of amniotic fluid volume (oligohydramnios) have been reported in pregnant women treated with non-steroidal anti-inflammatory drugs (NSAIDs) at 20 weeks of gestation or later. In some cases, this may result in neonatal renal dysfunction. Such effects may occur shortly after NSAID treatment initiation; oligohydramnios is often reversible after treatment discontinuation. Use of ARCOXIA is not recommended in pregnancy from 20 weeks of gestation onwards.

Reproductive studies conducted in rats and rabbits have demonstrated no evidence of

developmental abnormalities at doses up to 15 mg/kg/day (approximately 1.5 times the human dose [90 mg] based on systemic exposure). At doses approximately 2 times the adult human exposure (90 mg) based on systemic exposure, a low incidence of cardiovascular malformations and increases in post implantation loss were observed in etoricoxib-treated rabbits. No developmental effects were seen at systemic exposure of approximately equal to or less than the daily human dosage (90 mg). However, animal reproduction studies are not always predictive of human response. There are no adequate and well-controlled studies in pregnant women. ARCOXIA should be used during the first 20 weeks of pregnancy only if the potential benefit justifies the potential risk to the fetus.

NURSING MOTHERS

Etoricoxib is excreted in the milk of lactating rats. It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk and because of the possible adverse effects of drugs that inhibit prostaglandin synthesis on nursing infants, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

PEDIATRIC USE

Safety and effectiveness of etoricoxib in pediatric patients have not been established.

USE IN THE ELDERLY

Pharmacokinetics in the elderly (65 years of age and older) are similar to those in the young. In clinical studies, a higher incidence of adverse experiences was seen in older patients compared to younger patients; the relative differences between etoricoxib and control groups were similar in the elderly and the young. Greater sensitivity of some older individuals cannot be ruled out.

DRUG INTERACTIONS

Warfarin: In subjects stabilized on chronic warfarin therapy, the administration of ARCOXIA 120 mg daily was associated with an approximate 13% increase in prothrombin time International Normalized Ratio (INR). Standard monitoring of INR

values should be conducted when therapy with ARCOXIA is initiated or changed, particularly in the first few days, in patients receiving warfarin or similar agents.

Rifampin: Co-administration of ARCOXIA with rifampin, a potent inducer of hepatic metabolism, produced a 65% decrease in etoricoxib plasma area under the curve (AUC). This interaction should be considered when ARCOXIA is co-administered with rifampin.

Methotrexate: Two studies investigated the effects of ARCOXIA 60, 90 or 120 mg administered once daily for seven days in patients receiving once-weekly methotrexate doses of 7.5 to 20 mg for rheumatoid arthritis. ARCOXIA at 60 and 90 mg had no effect on methotrexate plasma concentrations (as measured by AUC) or renal clearance. In one study, ARCOXIA 120 mg had no effect on methotrexate plasma concentrations (as measured by AUC) or renal clearance. In the other study, ARCOXIA 120 mg increased methotrexate plasma concentrations by 28% (as measured by AUC) and reduced renal clearance of methotrexate by 13%. Monitoring for methotrexate-related toxicity should be considered when ARCOXIA at doses greater than 90 mg daily and methotrexate are administered concomitantly.

Diuretics, Angiotensin Converting Enzyme (ACE) Inhibitors and Angiotensin II Antagonists (AIIAs): Reports suggest that NSAIDs including selective COX-2 inhibitors may diminish the antihypertensive effect of diuretics, ACE inhibitors and AIIAs. This interaction should be given consideration in patients taking ARCOXIA concomitantly with these products.

In some patients with compromised renal function (e.g., elderly patients or patients who are volume-depleted, including those on diuretic therapy) who are being treated with non-steroidal anti-inflammatory drugs, including selective COX-2 inhibitors, the co-administration of ACE inhibitors or AIIAs may result in a further deterioration of renal function, including possible acute renal failure. These effects are usually reversible. Therefore, the combination should be administered with caution, especially in the elderly.

Lithium: Reports suggest that non-selective NSAIDs and selective COX-2 inhibitors may increase plasma lithium levels. This interaction should be given consideration in patients

taking ARCOXIA concomitantly with lithium.

Aspirin: ARCOXIA can be used concomitantly with low-dose aspirin at doses for cardiovascular prophylaxis. However, concomitant administration of low-dose aspirin with ARCOXIA results in an increased rate of GI ulceration or other complications compared to use of ARCOXIA alone. At steady state, etoricoxib 120 mg once daily had no effect on the anti-platelet activity of low-dose aspirin (81 mg once daily). (See PRECAUTIONS.)

Oral Contraceptives: ARCOXIA 60 mg given concomitantly with an oral contraceptive containing 35 mcg ethinyl estradiol (EE) and 0.5 to 1 mg norethindrone for 21 days increased the steady state $AUC_{0\text{-}24hr}$ of EE by 37%. ARCOXIA 120 mg given with the same oral contraceptive concomitantly or separated by 12 hours, increased the steady state $AUC_{0\text{-}24hr}$ of EE by 50 to 60%. This increase in EE concentration should be considered when selecting an oral contraceptive for use with etoricoxib. An increase in EE exposure can increase the incidence of adverse events associated with oral contraceptives (e.g., venous thrombo-embolic events in women at risk).

Hormone Replacement Therapy: Administration of ARCOXIA 120 mg with hormone replacement therapy consisting of conjugated estrogens (0.625 mg PREMARIN™) for 28 days, increased the mean steady state $AUC_{0\text{-}24hr}$ of unconjugated estrone (41%), equilin (76%), and 17-ß-estradiol (22%). The effect of the recommended chronic doses of ARCOXIA (60 and 90 mg) has not been studied. The effects of ARCOXIA 120 mg on the exposure ($AUC_{0\text{-}24hr}$) to these estrogenic components of PREMARIN were less than half of those observed when PREMARIN was administered alone and the dose was increased from 0.625 to 1.25 mg. The clinical significance of these increases is unknown, and higher doses of PREMARIN were not studied in combination with ARCOXIA. These increases in estrogenic concentration should be taken into consideration when selecting post-menopausal hormone therapy for use with ARCOXIA.

Other: In drug-interaction studies, ARCOXIA did not have clinically important effects on the pharmacokinetics of prednisone/prednisolone or digoxin.

Antacids and ketoconazole (a potent inhibitor of CYP3A4) did not have clinically

important effects on the pharmacokinetics of ARCOXIA.

SIDE EFFECTS

In clinical trials, ARCOXIA was evaluated for safety in approximately 9295 individuals, including 5774 patients with OA, RA or chronic low back pain (approximately 600 patients with OA or RA were treated for one year or longer).

The following drug-related adverse experiences were reported in clinical studies in patients with OA, RA, or chronic low back pain treated for up to 12 weeks. These occurred in ≥ 1% of patients treated with ARCOXIA and at an incidence greater than placebo: asthenia/fatigue, dizziness, lower extremity edema, hypertension, dyspepsia, heartburn, nausea, headache, ALT increased, AST increased.

The adverse experience profile was similar in patients with OA or RA treated with ARCOXIA for one year or longer.

In the MEDAL Study, an endpoint driven CV outcomes trial involving 23,504 patients, the safety of ARCOXIA 60 or 90 mg daily was compared to diclofenac 150 mg daily in patients with OA or RA (mean duration of treatment was 20 months). In this large trial, only serious adverse events and discontinuations due to any adverse events were recorded. The rates of confirmed thrombotic cardiovascular serious adverse events were similar between ARCOXIA and diclofenac. The incidence of discontinuations for hypertension-related adverse events was less than 3% in each treatment group; however, ARCOXIA 60 and 90 mg demonstrated significantly higher rates of discontinuations for these events than diclofenac. The incidence of congestive heart failure adverse events (discontinuations and serious events) and the incidence of discontinuations due to edema occurred at similar rates on ARCOXIA 60 mg compared to diclofenac; however, the incidences for these events were higher for ARCOXIA 90 mg compared to diclofenac. The incidence of discontinuations due to atrial fibrillation was higher for etoricoxib compared to diclofenac.

The EDGE and EDGE II studies compared the GI tolerability of etoricoxib 90 mg daily (1.5 to 3 times the doses recommended for OA) and diclofenac 150 mg daily in 7111 patients with OA (EDGE Study; mean duration of treatment 9 months) and 4086

patients with RA (EDGE II; mean duration of treatment 19 months). In each of these studies, the adverse experience profile on ARCOXIA was generally similar to that reported in the phase IIb/III placebo-controlled clinical studies; however, hypertension and edema related adverse experiences occurred at a higher rate on etoricoxib 90 mg than on diclofenac 150 mg daily. The rate of confirmed thrombotic cardiovascular serious adverse events occurring in the two treatment groups was similar.

In a combined analysis of phase IIb to V clinical studies of 4 weeks duration or longer (excluding the MEDAL Program Studies), there was no discernible difference in the rate of confirmed thrombotic cardiovascular serious adverse events between patients receiving etoricoxib ≥ 30 mg or non-naproxen NSAIDs. The rate of these events was higher in patients receiving etoricoxib compared with those receiving naproxen 500 mg twice daily.

In a clinical study for ankylosing spondylitis, patients were treated with ARCOXIA 90 mg once daily for up to 1 year (N=126). In another clinical study for ankylosing spondylitis (N=857), patients were treated with ARCOXIA 60 mg or 90 mg once daily for up to 26 weeks. The adverse experience profile in these studies was generally similar to that reported in chronic studies in OA, RA and chronic low back pain.

In a clinical study for acute gouty arthritis, patients were treated with ARCOXIA 120 mg once daily for eight days. The adverse experience profile in this study was generally similar to that reported in the combined OA, RA, and chronic low back pain studies.

In initial clinical studies for acute analgesia, patients were treated with ARCOXIA 120 mg once daily for one to seven days. The adverse experience profile in these studies was generally similar to that reported in the combined OA, RA, and chronic low back pain studies.

In additional clinical studies for acute post-operative pain including 1222 patients treated with ARCOXIA (90 mg or 120 mg), the adverse experience profile was generally similar to that reported in the combined OA, RA, and chronic low back pain studies.

In the combined studies for acute post-operative dental pain, the incidence of post-dental extraction alveolitis (dry socket) reported in patients treated with ARCOXIA was similar to that of patients treated with active comparators.

Post-marketing experience

The following adverse reactions have been reported in post-marketing experience:

Blood and lymphatic system disorders: thrombocytopenia.

Immune system disorders: hypersensitivity reactions, including anaphylactic/anaphylactoid reactions including shock.

Metabolism and nutrition disorders: hyperkalemia.

Psychiatric disorders: anxiety, insomnia, confusion, hallucinations, depression, restlessness.

Nervous system disorders: dysgeusia, somnolence, intracranial hemorrhage.

Eye disorders: blurred vision.

Cardiac disorders: congestive heart failure, palpitations, angina, arrhythmia.

Vascular disorders: hypertensive crisis, deep vein thrombosis.

Respiratory, thoracic and mediastinal disorders: bronchospasm, pulmonary embolism.

Gastrointestinal disorders: abdominal pain, oral ulcers, peptic ulcers including perforation and bleeding (mainly in elderly patients), vomiting, diarrhea.

Hepatobiliary disorders: hepatitis, jaundice, hepatic failure.

Skin and subcutaneous tissue disorders: angioedema, pruritus, erythema, rash, Stevens-Johnson syndrome, toxic epidermal necrolysis, urticaria, fixed drug eruption.

Renal and urinary disorders: renal insufficiency, including renal failure (see PRECAUTIONS).

OVERDOSAGE

In clinical studies, administration of ARCOXIA at single doses up to 500 mg and multiple doses up to 150 mg/day for 21 days did not result in significant toxicity. There have been reports of acute overdosage with etoricoxib, although adverse experiences were not reported in the majority of cases. The most frequently observed adverse experiences were consistent with the safety profile for etoricoxib (e.g. gastrointestinal events, renovascular events).

In the event of overdose, it is reasonable to employ the usual supportive measures, e.g.,

remove unabsorbed material from the gastrointestinal tract, employ clinical monitoring, and institute supportive therapy, if required.

Etoricoxib is not dialyzable by hemodialysis; it is not known whether etoricoxib is dialyzable by peritoneal dialysis.

CLINICAL PHARMACOLOGY

Mechanism of Action

Etoricoxib is a nonsteroidal anti-inflammatory drug (NSAID) that exhibits anti-inflammatory, analgesic, and antipyretic activities in animal models. Etoricoxib is a potent, orally active, highly selective cyclooxygenase-2 (COX-2) inhibitor within and above the clinical dose range. Two isoforms of cyclooxygenase have been identified: cyclooxygenase-1 (COX-1) and cyclooxygenase-2 (COX-2). COX-1 is responsible for prostaglandin-mediated normal physiologic functions such as gastric cytoprotection and platelet aggregation. Inhibition of COX-1 by nonselective NSAIDs has been associated with gastric damage and platelet inhibition. COX-2 has been shown to be primarily responsible for the synthesis of prostanoid mediators of pain, inflammation, and fever. Selective inhibition of COX-2 by etoricoxib decreases these clinical signs and symptoms with decreased GI toxicity and without effects on platelet function.

Across clinical pharmacology studies, etoricoxib produced dose-dependent inhibition of COX-2 without inhibition of COX-1 at doses up to 150 mg daily.

The influence on gastroprotective COX-1 activity was also assessed in a clinical study where prostaglandin synthesis was measured in gastric biopsy samples from subjects administered either etoricoxib 120 mg daily, naproxen 500 mg twice daily, or placebo. Etoricoxib did not inhibit gastric prostaglandin synthesis as compared to placebo. In contrast, naproxen inhibited gastric prostaglandin synthesis by approximately 80% compared with placebo. These data further support the COX-2 selectivity of etoricoxib.

Platelet Function

Multiple doses of etoricoxib up to 150 mg administered daily up to nine days had no effect on bleeding time relative to placebo. Similarly, bleeding time was not altered in a single-dose study with etoricoxib 250 or 500 mg. There was no inhibition of *ex vivo*

arachidonic acid- or collagen-induced platelet aggregation at steady state with doses of ARCOXIA up to 150 mg. These findings are consistent with the COX-2 selectivity of etoricoxib.

Pharmacokinetics

1. Absorption

Orally administered etoricoxib is well absorbed. The mean oral bioavailability is approximately 100%. Following 120 mg once-daily dosing to steady state, the peak plasma concentration (geometric mean C_{max} = 3.6 mcg/mL) was observed at approximately 1 hour (T_{max}) after administration to fasted adults. The geometric mean AUC_{0-24hr} was 37.8 mcg• hr/mL. The pharmacokinetics of etoricoxib are linear across the clinical dose range.

A standard meal had no clinically meaningful effect on the extent or rate of absorption of a dose of etoricoxib 120 mg. In clinical trials, etoricoxib was administered without regard to food.

The pharmacokinetics of etoricoxib in 12 healthy subjects were similar (comparable AUC, C_{max} within approximately 20%) when administered alone, with a magnesium/aluminum hydroxide antacid, or a calcium carbonate antacid (approximately 50 mEq acid-neutralizing capacity).

2. Distribution

Etoricoxib is approximately 92% bound to human plasma protein over the range of concentrations of 0.05 to 5 mcg/mL. The volume of distribution at steady state (V_{dss}) is approximately 120 L in humans.

Etoricoxib crosses the placenta in rats and rabbits, and the blood-brain barrier in rats

3. Metabolism

Etoricoxib is extensively metabolized with <1% of a dose recovered in urine as the

parent drug. The major route of metabolism to form the 6'-hydroxymethyl derivative is catalyzed by cytochrome P450 (CYP) enzymes.

Five metabolites have been identified in man. The principal metabolite is the 6'-carboxylic acid derivative of etoricoxib formed by further oxidation of the 6'-hydroxymethyl derivative. These principal metabolites either demonstrate no measurable activity or are only weakly active as COX-2 inhibitors. None of these metabolites inhibit COX-1.

4. Elimination

Following administration of a single 25 mg radiolabeled intravenous dose of etoricoxib to healthy subjects, 70% of radioactivity was recovered in urine and 20% in feces, mostly as metabolites. Less than 2% was recovered as unchanged drug.

Elimination of etoricoxib occurs almost exclusively through metabolism followed by renal excretion. Steady state concentrations of etoricoxib are reached within seven days of once-daily administration of 120 mg, with an accumulation ratio of approximately 2, corresponding to an accumulation half-life of approximately 22 hours. The plasma clearance is estimated to be approximately 50 mL/min.

5. Characteristics in Patients (Special Populations)

Gender

The pharmacokinetics of etoricoxib are similar between men and women. (See DOSAGE AND ADMINISTRATION.)

Elderly

Pharmacokinetics in the elderly (65 years of age and older) are similar to those in the young. No dosage adjustment is necessary for elderly patients. (See DOSAGE AND ADMINISTRATION.)

Race

There is no clinically important effect of race on the pharmacokinetics of etoricoxib. (See DOSAGE AND ADMINISTRATION.)

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Hepatic Insufficiency

Patients with mild hepatic insufficiency (Child-Pugh score 5-6) administered etoricoxib 60 mg once daily had an approximately 16% higher mean AUC as compared to healthy subjects given the same regimen. Patients with moderate hepatic insufficiency (Child-Pugh score 7-9) administered etoricoxib 60 mg ***every other day*** had similar mean AUC to the healthy subjects given etoricoxib 60 mg once daily. There are no clinical or pharmacokinetic data in patients with severe hepatic insufficiency (Child-Pugh score >9). (See DOSAGE AND ADMINISTRATION, *Hepatic Insufficiency.*)

Renal Insufficiency

The pharmacokinetics of a single dose of etoricoxib 120 mg in patients with moderate-to-severe renal insufficiency and patients with end-stage renal disease on hemodialysis were not significantly different from those in healthy subjects. Hemodialysis contributed negligibly to elimination (dialysis clearance approximately 50 mL/min).

Pediatric Patients

The pharmacokinetics of etoricoxib in pediatric patients (<12 years of age) have not been studied.

In a pharmacokinetic study (N=16) conducted in adolescents (aged 12 to 17) the pharmacokinetics in adolescents weighing 40 to 60 kg given etoricoxib 60 mg once daily and in adolescents >60 kg given etoricoxib 90 mg once daily were similar to the pharmacokinetics in adults given etoricoxib 90 mg once daily. Safety and effectiveness of etoricoxib in pediatric patients have not been established.

ANIMAL TOXICOLOGY

ACUTE TOXICITY

The approximate oral LD_{50} was 1499 mg/kg in both female mice and rats, while the intraperitoneal approximate oral LD_{50} was 599 mg/kg in female mice and 238 mg/kg in female rats. The approximate oral LD_{50} in rats and mice are >12 times the acute daily adult human dose [120 mg] based on systemic exposure.

CHRONIC TOXICITY

The toxicity potential of etoricoxib was evaluated in a series of repeated-dose oral toxicity studies up to 53 weeks in dogs and rats. In each species, the principal treatment-related changes were associated with renal and gastrointestinal toxicity. Both the renal and gastrointestinal lesions were shown to occur at dosages above the intended chronic clinical dose of 90 mg daily.

In dogs administered etoricoxib orally at dosages of 200 mg/kg/day (approximately 20 times the daily adult human dose [90 mg] based on systemic exposure) for 14 weeks, toxicity was characterized by gastritis, gastrointestinal ulceration and renal papillary necrosis. No toxicity was seen in dogs administered 50 mg/kg/day (approximately 3 times the daily adult human dose based on systemic exposure) for 53 weeks.

In rats, etoricoxib administered orally at dosages of 30 mg/kg/day (approximately 3 times the daily adult human dose [90 mg] based on systemic exposure) following 27 weeks of administration produced gastrointestinal ulceration, as well as increased hepatic weights in female rats. At 53 weeks, the increased hepatic weights observed correlated with centrilobular hepatocellular hypertrophy due to hepatic CYP enzyme induction. No renal or gastrointestinal changes were noted in rats administered 10 mg/kg/day for 53 weeks (approximately equivalent to the daily adult human dose based on systemic exposure).

CARCINOGENICITY

Etoricoxib was not carcinogenic in mice. Rats developed hepatocellular and thyroid follicular cell adenomas at >6 times the daily human dose [90 mg] based on systemic exposure when dosed daily for approximately 2 years. Tumors of these types are a species-specific consequence of hepatic CYP enzyme induction in the rat. These findings are consistent with other compounds associated with this induction. Etoricoxib has not been shown to cause hepatic CYP enzyme induction in humans.

MUTAGENESIS

Etoricoxib was found to be neither genotoxic nor mutagenic as described below. Etoricoxib was negative in the *in vitro* microbial and the TK6 human cell mutagenesis assays, with and without metabolic activation. There was no evidence of genotoxicity in the *in vitro* alkaline elution assay in rat hepatocytes and the *in vitro* chromosomal

aberration assays in Chinese hamster ovary cells, with or without metabolic activation. In the *in vivo* alkaline elution/rat liver damage assays, etoricoxib did not induce DNA strand breaks in rat liver cells after oral administration of doses up to 300 mg/kg (1770 mg/m^2; >20 times the daily adult dose [90 mg] based on systemic exposure). Similarly, there was no induction of chromosomal aberrations in bone marrow cells of male or female mice after the administration of oral doses of up to 1000 mg/kg (3000 mg/m^2; approximately 10 times the daily adult dose [90 mg] based on systemic exposure).

REPRODUCTION

In female rats administered etoricoxib, there were no adverse effects for maternotoxicity, fertility and embryonic/fetal survival at dosages of 10 mg/kg/day (approximately equivalent to the daily adult human dose [90 mg] based on systemic exposure). At dosages of 30 mg/kg/day (approximately 3 times the daily adult human dose [90 mg] based on systemic exposure), there were treatment-related decreases in the number of implants.

High placental transfer of etoricoxib occurred in rabbits treated with 45 mg/kg/day (approximately 3 times the daily adult human dose [90 mg] based on systemic exposure), as evidenced by rabbit fetal plasma levels of approximately 60 to 70% of the mean maternal plasma drug levels. In pregnant rats treated with 15 mg/kg/day (approximately 1.5 times the daily adult human dose [90 mg] based on systemic exposure), there was approximately 70 to 80% placental transfer of etoricoxib.

Significant concentrations of etoricoxib were observed in the milk of lactating rats. The mean milk drug concentrations were approximately two-fold the mean maternal plasma concentrations in rats administered doses up to 15 mg/kg/day (approximately 1.5 times the daily adult human dose [90 mg] based on systemic exposure).

There were no treatment-related effects on mating performance, fertility indices, embryonic/fetal survival, sperm count, motility, testicular/epididymal organ weights, or histology in male rats administered dosages of etoricoxib up to 100 mg/kg/day (>6 times the daily adult human dose [90 mg] based on systemic exposure).

DEVELOPMENT

No teratogenic effects were observed in rabbits and rats administered etoricoxib at

doses up to 10 and 15 mg/kg/day, respectively (approximately equal to and approximately 1.5 times, respectively, the daily adult human dose [90 mg] based on systemic exposure). At doses approximately 2 times the adult human exposure (90 mg) based on systemic exposure, a low incidence of cardiovascular malformations and increases in post implantation loss were observed in etoricoxib-treated rabbits. No developmental effects were seen at systemic exposure of approximately equal to or less than the daily human dosage (90mg).

Effects on ability to drive and use machines

There is no information to suggest that ARCOXIA affects a patient's ability to drive or operate machinery.

Storage condition

Store below 30^{o}C

If there is any adverse events please inform to

PT Organon Pharma Indonesia Tbk, Jakarta. Telephone : (021) 31107001; Email : dpoc.indonesia@organon.com

Presentation

ARCOXIA 60 mg Film Coated Tablet, available in box of 3 blister @ 10 tablets

Reg.No.: DKL1906609417A1

ARCOXIA 90 mg Film Coated Tablet, available in box of 3 blister @ 10 tablets

Reg.No.: DKL1906609417B1

ARCOXIA 120 mg Film Coated Tablet, available in box of 3 blister @ 10 tablets

Reg.No.: DKL1906609417C1

HARUS DENGAN RESEP DOKTER

Manufactured by:

Rovi Pharma Industrial Services S.A.

Via Complutense, 140

28805 - Alcala de Henares, Madrid, Spain

Registered and Packed by:

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PT Organon Pharma Indonesia Tbk

Pasuruan, Jawa Timur

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Informasi Untuk Pasien

Tentang ARCOXIA™

Harap baca leaflet ini dengan seksama sebelum anda mulai minum obat ini, walau anda telah menggunakan obat ini sebelumnya. Beberapa informasi dalam leaflet sebelumnya dapat berubah.
Ingatlah bahwa dokter anda meresepkan obat ini hanya untuk anda. Jangan berikan kepada orang lain.

Apakah ARCOXIA?

ARCOXIA (etoricoxib) adalah tablet yang mengandung 60, 90, atau 120 mg etoricoxib sebagai bahan aktif.

ARCOXIA merupakan senyawa kimia dari golongan obat yang disebut coxib yang digunakan untuk mengurangi rasa sakit dan peradangan. ARCOXIA adalah selektif COX-2 inhibitor. ARCOXIA bukan narkotika.

Didaftarkan oleh:
PT Organon Pharma Indonesia Tbk
Pasuruan, Jawa Timur

Produsen:
Rovi Pharma Industrial Services S.A.
Via Complutense, 140
28805 - Alcala de Henares, Madrid, Spain

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Mengapa dokter saya meresepkan ARCOXIA?

Dokter Anda telah memberikan resep ARCOXIA untuk:

- Meringankan gejala dalam pengobatan ostheoarthritis (OA) dan rheumatoid arthritis (RA)
- Meringankan gejala dalam pengobatan ankylosing spondylitis (AS)
- Pengobatan nyeri dan gejala peradangan yang terkait dengan arthritis gout akut. ARCOXIA harus digunakan hanya untuk periode gejala akut dibatasi maksimal 8 hari.
- Meringankan nyeri muskuloskeletal kronis
- Meringankan nyeri akut berhubungan dengan operasi gigi.

Bagaimana cara kerja ARCOXIA?

Tubuh menghasilkan dua enzim serupa yang disebut COX-1 dan COX-2. COX-1, fungsi antara lain adalah terlibat dalam melindungi perut, sedangkan COX 2 berperan dalam peradangan dan nyeri sendi.

- ARCOXIA mengurangi rasa sakit dan peradangan dengan menghambat COX-2, suatu zat dalam tubuh
- ARCOXIA tidak menghalangi COX-1, zat terkait yang terlibat dalam melindungi perut dari ulkus.
- Obat anti-inflamasi lainnya (NSAID) memblokir keduanya, baik COX-1 dan COX-2.
- ARCOXIA mengurangi rasa sakit dan peradangan dengan sedikit risiko terjadinya ulkus dibandingkan dengan NSAIDs .

Apa Osteoarthritis?

Osteoarthritis merupakan penyakit sendi, hasil dari pemecahan bertahap tulang rawan yang melindungi ujung tulang, sehingga terjadi nyeri, peradangan, kerapuhan, kekakuan, dan cacat fisik.

Apa Rheumatoid Arthritis?

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Rheumatoid Arthritis adalah penyakit kronis yang menyebabkan nyeri, kekakuan, melepuh dan kehilangan fungsi dari otot dan peradangan pada organ tubuh lain.

Apa Ankylosing Spondylitis?

Ankylosing Spondylitis adalah penyakit peradangan pada tulang belakang dan sendi besar.

Apa itu Gout?

Gout adalah gangguan yang ditandai dengan tiba-tiba, serangan berulang dari nyeri dan peradangan pada satu atau lebih sendi.

Apa lagi yang bisa saya lakukan untuk membantu mengelola arthritis saya?

Bicaralah dengan dokter Anda tentang :

- Olah raga
- Mengontrol berat badan Anda
- Perawatan panas dan dingin
- Menggunakan perangkat pendukung.

Apa yang harus saya ketahui sebelum mengambil ARCOXIA?

Siapa yang tidak boleh menggunakan ARCOXIA?

Jangan menggunakan ARCOXIA jika Anda :

- Alergi terhadap salah satu komponennya.
- Memiliki gagal jantung, serangan jantung, operasi bypass, nyeri dada (angina), penyakit arteri perifer, stroke atau mini stroke (TIA atau *transient ischemic attack*)

Apa yang harus kukatakan dokter saya sebelum menggunakan ARCOXIA?

Beritahukan kepada dokter anda (atau penyedia layanan kesehatan) mengenai masalah medis atau alergi apapun yang anda miliki, termasuk:

- Riwayat angina, serangan jantung atau arteri yang tersumbat di dalam hati Anda.
- Arteri sempit atau diblokir dari ekstremitas.
- Penyakit ginjal

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- Penyakit hati
- Dehidrasi, misalnya karena berkepanjangan muntah atau diare.
- Riwayat perdarahan lambung atau tukak.
- Gagal jantung
- Tekanan darah tinggi
- Bengkak karena retensi cairan.
- Reaksi alergi terhadap aspirin atau obat anti-inflamasi lainnya (umumnya dikenal sebagai NSAID).
- Riwayat stroke atau stroke mini.
- Kondisi yang meningkatkan risiko penyakit arteri koroner atau aterosklerosis seperti tekanan darah tinggi, diabetes, kolesterol tinggi atau merokok.
- Sedang dirawat karena infeksi. ARCOXIA dapat menutupi atau menyembunyikan demam, yang merupakan tanda infeksi.

Apa lagi yang harus saya ketahui tentang ARCOXIA?

- Dalam studi klinis, risiko terjadinya ulkus pada ARCOXIA lebih rendah dibandingkan dengan NSAID. Beberapa orang mengalami ulkus pada saat menggunakan ARCOXIA atau plasebo dalam studi ini; namun, jumlahnya lebih lebih tinggi pada ARCOXIA .
- Jika salah satu gejala berikut: sesak napas ,nyeri dada atau pergelangan kaki bengkak muncul atau memburuk, hentikan pengobatan dengan ARCOXIA dan berkonsultasi dengan dokter, sesegera mungkin.
- Jika Anda memiliki penyakit ginjal, penyakit hati atau penyakit jantung, mintalah dokter Anda untuk mengecek secara tepat.
- Jika Anda mengalami gejala-gejala yang bisa menunjukkan reaksi alergi parah seperti ketidakmampuan untuk bernapas atau reaksi kulit yang serius, Anda harus berkonsultasi dengan dokter segera.
- Dokter Anda mungkin ingin membahas perawatan Anda dari waktu ke waktu. Penting bahwa Anda menggunakan dosis terendah untuk mengontrol rasa sakit Anda dan Anda tidak harus mengambil ARCOXIA lebih lama dari yang diperlukan. Hal ini karena risiko serangan jantung dan stroke mungkin meningkat setelah pengobatan jangka panjang, terutama dengan dosis tinggi.

- ARCOXIA dapat meningkatkan tekanan darah pada beberapa orang, terutama dalam dosis tinggi, dan hal ini bisa meningkatkan risiko serangan jantung dan stroke. Dokter Anda akan memeriksa tekanan darah Anda dari waktu ke waktu, untuk memastikan bahwa itu aman untuk melanjutkan pengobatan.

Penggunaan pada anak-anak

ARCOXIA belum cukup diteliti pada anak-anak. Oleh karena itu, ARCOXIA tidak boleh diberikan kepada anak-anak.

Penggunaan pada orang tua

ARCOXIA bekerja secara baik pasien dewasa yang lebih tua dan lebih muda. Efek samping bisa terjadi dengan angka kejadian yang lebih tinggi pada pasien yang lebih tua dibandingkan dengan pasien yang lebih muda. Jika Anda sudah berusia lanjut (yaitu, lebih dari 65 tahun), dokter Anda akan mengecek secara tepat. Tidak ada penyesuaian dosis diperlukan untuk pasien yang lebih tua.

Penggunaan pada kehamilan dan menyusui

Katakan kepada dokter Anda jika Anda:

- Hamil atau berencana untuk hamil.
- ARCOXIA sebaiknya tidak digunakan dari kehamilan 20 minggu dan seterusnya karena dapat membahayakan janin.
- Menyusui atau berencana untuk menyusui.

Dapatkah saya mengambil ARCOXIA dengan obat lain?

Anda harus selalu memberitahu dokter Anda tentang semua obat yang Anda pakai atau rencana untuk memakai, termasuk yang diperoleh tanpa resep.

Dokter Anda mungkin ingin memeriksa bahwa obat Anda bekerja dengan baik jika Anda menggunakan:

- Warfarin (pengencer darah)
- Rifampisin (antibiotik)
- Diuretik

- ACE inhibitor dan *angiotensin receptor blocker* (obat yang digunakan untuk tekanan darah tinggi dan gagal jantung)
- Lithium (obat yang digunakan untuk mengobati jenis tertentu depresi)
- Pil KB
- Terapi hormon pengganti
- Methotrexate (obat yang digunakan untuk menekan sistem kekebalan tubuh).

ARCOXIA dapat digunakan bersamaan dengan aspirin dosis rendah. Jika Anda saat ini sedang menggunakan aspirin dosis rendah untuk pencegahan serangan jantung atau stroke, Anda tidak harus menghentikan tanpa berkonsultasi dengan dokter Anda karena ARCOXIA tidak dapat menggantikan aspirin untuk tujuan ini.

Dapatkah saya mengemudi atau mengoperasikan mesin saat menggunakan ARCOXIA?

Tidak ada informasi yang menunjukkan bahwa ARCOXIA mempengaruhi kemampuan Anda untuk mengemudi atau mengoperasikan mesin.

Apa yang harus saya tahu tentang bahan-bahan aktif dalam ARCOXIA ?

ARCOXIA 60 mg tablet mengandung 2,8 mg laktosa, ARCOXIA 90 mg tablet mengandung 4,2 mg laktosa, dan ARCOXIA 120 mg tablet mengandung 5,6 mg laktosa.

Bagaimana saya menggunakan ARCOXIA?

ARCOXIA diminum sekali sehari. Anda dapat menggunakan ARCOXIA dengan atau tanpa makanan.

Dokter Anda akan memutuskan berapa dosis ARCOXIA harus Anda minum dan berapa lama Anda harus menggunakannya.

Untuk pengobatan osteoarthritis

Dosis yang dianjurkan adalah 60 mg sekali sehari.

Untuk pengobatan rheumatoid arthritis

Dosis yang dianjurkan adalah 60 mg sekali sehari. Pada beberapa pasien dengan gejala yang tidak cukup mereda, peningkatan dosis menjadi 90 mg sekali sehari dapat meningkatkan kemanjuran.

Untuk pengobatan ankylosing spondylitis
Dosis yang dianjurkan adalah 60 mg sekali sehari. Pada beberapa pasien dengan gejala yang tidak cukup mereda, peningkatan dosis menjadi 90 mg sekali sehari dapat meningkatkan kemanjuran.

Untuk pasca operasi gigi
Dosis yang dianjurkan adalah 90 mg sekali sehari.

Untuk pengobatan arthritis gout akut
Dosis yang dianjurkan adalah 120 mg sekali sehari. ARCOXIA harus digunakan hanya untuk periode gejala akut dibatasi maksimal 8 hari.

Untuk pengobatan nyeri muskuloskeletal kronis
Dosis yang dianjurkan adalah 60 mg sekali sehari.

Dosis lebih besar dari yang direkomendasikan untuk setiap kondisi tidak menunjukkan tambahan keberhasilan atau belum diteliti. Oleh karena itu, dosis harian yang disebutkan di atas untuk setiap kondisi tidak seharusnya dilampaui.

Jika Anda memiliki penyakit hati ringan, Anda tidak seharusnya menggunakan dosis lebih dari 60 mg per hari. Jika Anda memiliki penyakit hati yang moderat, Anda tidak seharusnya menggunakan dosis lebih lebih dari 60 mg setiap hari.

Jangan berbagi ARCOXIA dengan orang lain; ARCOXIA diresepkan hanya untuk Anda.

Apa yang harus saya lakukan bila terjadi overdosis?
Jika Anda mengambil lebih dari dosis yang diresepkan, segera hubungi dokter Anda.

Apa yang harus saya lakukan jika saya melewatkan satu dosis?

Cobalah untuk mengambil ARCOXIA seperti yang ditentukan. Namun, jika Anda melewatkan dosis, jangan mengambil dosis ekstra. Hanya melanjutkan jadwal biasa Anda pada hari berikutnya.

Apa efek samping yang mungkin ARCOXIA miliki?

Setiap obat mungkin memiliki efek yang tidak diinginkan atau tidak diinginkan, yang disebut efek samping.

Seperti semua obat resep, ARCOXIA dapat menyebabkan efek samping. Dalam penelitian, efek samping biasanya ringan. Mereka umumnya tidak menyebabkan pasien untuk menghentikan minum ARCOXIA.

Beberapa efek samping yang dilaporkan dalam studi meliputi: pusing, pembengkakan pada kaki dan/ atau kaki, kelemahan dan kelelahan, tekanan darah tinggi, mual, mulas, sakit kepala, sakit perut dan *dry socket* (peradangan dan nyeri setelah pencabutan gigi).

Selain itu, berikut telah dilaporkan: reaksi alergi (yang mungkin cukup serius untuk meminta perhatian medis segera) termasuk pembengkakan wajah, bibir, lidah, dan/atau tenggorokan yang dapat menyebabkan kesulitan bernafas atau menelan, mengi, ruam, gatal-gatal; kemerahan pada kulit, reaksi kulit yang parah yang mungkin terjadi tanpa gejala; perubahan selera, irama jantung yang tidak normal (aritmia), gagal jantung, palpitasi, rasa sesak, tekanan atau rasa berat di dada (angina), sakit perut, sakit maag yang dapat menjadi serius dan dapat berdarah dan dapat terjadi setiap saat selama penggunaan dan tanpa gejala, muntah, masalah hati termasuk gagal hati, kulit dan mata menguning (jaundice), masalah ginjal yang serius, kadar kalium yang tinggi dalam darah Anda, insomnia, kecemasan, depresi, kegelisahan, mengantuk, sariawan, diare, peningkatan berat tekanan darah, kebingungan, halusinasi, trombosit menurun, penglihatan kabur, pembekuan darah di pembuluh darah paru-paru dan/atau kaki, dan pendarahan di dalam otak.

Efek samping lain juga dapat terjadi jarang, dan sama dengan obat resep lainnya, beberapa efek samping mungkin serius. Tanyakan kepada dokter atau apoteker untuk informasi lebih

lanjut. Keduanya memiliki daftar yang lebih lengkap. Beritahu dokter atau apoteker Anda segera tentang hal ini atau gejala yang tidak biasa lainnya.

Bagaimana saya bisa belajar lebih banyak tentang ARCOXIA, osteoarthritis, rheumatoid arthritis, ankylosing spondylitis, gout, dan nyeri?

Anda dapat memperoleh informasi lebih lanjut dari dokter atau apoteker, yang memiliki informasi lebih rinci.

Berapa lama saya harus menyimpan obat saya?

Jangan gunakan obat ini setelah bulan dan tahun yang ditunjukkan oleh EXP pada kemasan. Dua angka pertama menunjukkan bulan; empat angka terakhir menunjukkan tahun.

Bagaimana seharusnya saya menyimpan ARCOXIA?

Simpan ARCOXIA bawah suhu 30°C

Jauhkan ARCOXIA dan semua obat dari jangkauan anak-anak.

Apabila ada keluhan efek samping, silakan hubungi PT Organon Pharma Indonesia Tbk, Jakarta. Telepon : (021) 31107001; Email : dpoc.indonesia@organon.com

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