PROFESSIONAL INFORMATION

SCHEDULING STATUS

S3

1. NAME OF THE MEDICINE

ECOXAR 30 mg Film coated tablets

ECOXAR 60 mg Film coated tablets

ECOXAR 90 mg Film coated tablets

ECOXAR 120 mg Film coated tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

ECOXAR 30 mg

Each film coated tablet contains etoricoxib 30 mg.

Contains sugar: lactose monohydrate 1,05 mg/coated tablet.

ECOXAR 60 mg

Each film coated tablet contains etoricoxib 60 mg.

Contains sugar: lactose monohydrate 2,10 mg/coated tablet.

ECOXAR 90 mg

Each film coated tablet contains etoricoxib 90 mg.

Contains sugar: lactose monohydrate 3,15 mg/coated tablet.

ECOXAR 120 mg

Each film coated tablet contains etoricoxib 120 mg.

Contains sugar: lactose monohydrate 4,20 mg/coated tablet.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

ECOXAR 30 mg

Blue green, film coated, round biconvex tablets, E30 debossed on one side and plain on other side.

ECOXAR 60 mg

Green to dark green, film coated, round biconvex tablets, E60 debossed on one side and plain on other side.

ECOXAR 90 mg

White to off white, film coated, round biconvex tablets, E90 debossed on one side and plain on other side.

ECOXAR 120 mg

Light green to pale green, film coated round biconvex tablets, E120
debossed on one side and plain on other side.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

ECOXAR is indicated for:

- symptomatic relief of osteoarthritis (OA) and rheumatoid arthritis (RA).
- treatment of ankylosing spondylitis (AS).
- treatment of acute gouty arthritis.
- short term relief of acute pain, treatment limited to a maximum period of 8 days.
- treatment of primary dysmenorrhoea.
- treatment of moderate to severe acute post-operative 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 section 4.4).

4.2 Posology and method of administration

Posology

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

Osteo-arthritis (OA): The recommended dose is 30 mg* once daily. In some patients with insufficient relief from symptoms, the dose may be increased to 60 mg once daily.

Rheumatoid Arthritis (RA): The recommended dose is 90 mg once daily. In some patients, 60 mg once daily may provide adequate therapeutic benefit.

Ankylosing Spondylitis: The recommended dose is 90 mg once daily. In some patients, 60 mg once daily may provide adequate therapeutic benefit.

Short term relief of Acute Pain: The recommended dose is 90 mg or 120 mg once daily, limited to a maximum of 8 days treatment.

Acute Gouty Arthritis: The recommended dose is 120 mg once daily, limited to a maximum of 8 days treatment.

Primary Dysmenorrhoea: The recommended dose is 120 mg once daily.

Post-operative Dental Pain: The recommended dose is 90 mg once daily.

Doses greater than those recommended for each indication have either not demonstrated additional efficacy or have not been studied.

Therefore:

The dose for OA should not exceed 60 mg daily.

The dose for RA should not exceed 90 mg daily.

The dose for ankylosing spondylitis should not exceed 90 mg daily.

The dose for acute gout should not exceed 120 mg daily.

The dose for acute pain and primary dysmenorrhoea should not exceed 120 mg daily.

The dose for postoperative acute dental surgery pain should not exceed

90 mg daily.

As the cardiovascular risks of ECOXAR may increase with dose and duration of exposure, the shortest duration possible and the lowest effective daily dose should be used. The patient's need for symptomatic relief and response to therapy should be re-evaluated periodically (see section 4.4.).

Special populations

Elderly

No dosage adjustment in ECOXAR is necessary for the elderly. Although the elderly may be more susceptible to renal, gastrointestinal and cardiovascular adverse effects (see section 4.4). When using ECOXAR in the elderly and in patients with renal, hepatic or cardiac dysfunction, medically appropriate supervision should be intensified.

If these patients show deterioration during treatment, appropriate measures should be taken, including discontinuation of ECOXAR.

Hepatic Insufficiency

In patients with mild hepatic insufficiency (Child Pugh score 5 to 6), a dose of 60 mg once daily should not be exceeded.

In patients with moderate hepatic insufficiency (Child-Pugh score 7 to 9), the dose should be reduced; a dose of 60 mg every other day should not be exceeded, administration of ECOXAR 30 mg* once daily can also be considered.

Clinical experience is limited particularly in patients with moderate hepatic dysfunction. There are no clinical or pharmacokinetic data in patients with severe hepatic insufficiency (Child-Pugh

score > 9), therefore the use of ECOXAR is contraindicated in these patients (see section 4.3 and 5.2)

Renal Insufficiency

No dosage adjustment is necessary for patients with lesser degrees of renal insufficiency (creatinine clearance ≥ 30 mL/min). The use of ECOXAR in patients with creatinine clearance < 30 mL/min is contraindicated (see section 4.3).

When using ECOXAR in the elderly and in patients with renal, hepatic or cardiac dysfunction, medically appropriate supervision should be intensified. If patients show deterioration during treatment, appropriate measures should be taken, including discontinuation of ECOXAR.

4.3 Contraindications

ECOXAR is contraindicated in:

- patients with known hypersensitivity to any of the excipients of ECOXAR (see section 6.1)
- patients with active peptic ulceration or gastrointestinal (GI) bleeding
- patients with severe hepatic dysfunction (Child-Pugh score > 9 or serum albumin < 25 g/litre)
- patients with estimated creatinine clearance < 30 mL/min
- patients who have developed signs of asthma, acute rhinitis, nasal polyps, angioedema or urticaria following the administration of aspirin or other non-steroidal anti-inflammatory drugs (NSAIDs) including etoricoxib, as contained in ECOXAR
- uncontrolled hypertension
- pregnancy and lactation, avoid prescribing NSAIDs such as ECOXAR after 20 weeks as it may cause rare kidney problems in unborn babies (see section 4.4)
- children and adolescents under 16 years of age
- patients with inflammatory bowel disease

- patients with congestive heart failure (NYHA II -IV)
- established ischaemic heart disease, peripheral arterial disease and/or cerebrovascular disease (see section 4.4).
- peri-operative analgesia in the setting of coronary artery bypass surgery (CABG).
- Lithium therapy

  Concomitant administration with ECOXAR may lead to toxic blood concentration of lithium (see section 4.5)
- Digoxin

  There was an approximate increase of 33 % in the digoxin C_{max} in healthy volunteers (see section 4.5)

4.4 Special warning an precautions for use

ECOXAR may predispose to cardiovascular events, gastrointestinal events or cutaneous reactions which may be fatal.

Clinical trials suggest that the selective COX-2 inhibitor class of medicines, such as ECOXAR, are associated with an increased risk of arterial thrombotic events (especially myocardial infarction (MI)) and stroke).

Long-term administration of NSAIDs such as ECOXAR, has resulted in renal papillary necrosis and other renal injury. Renal prostaglandins may play a compensatory role in the maintenance of renal perfusion. Therefore, under conditions of compromised renal perfusion, administration of ECOXAR 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 liver cirrhosis. Monitoring of renal and hepatic function in such patients is indicated.

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

Fluid retention, oedema and hypertension have been reported in patients taking ECOXAR. All non-steroidal anti-inflammatory drugs (NSAIDs), including ECOXAR, can be associated with new onset or recurrent congestive heart failure. Caution should be exercised in patients with a history of cardiac failure, left ventricular dysfunction or hypertension, and in patients with pre-existing oedema from any other reason. If there is clinical evidence of deterioration in the condition of these patients, appropriate measures including discontinuation of ECOXAR should be taken.

ECOXAR may be associated with more frequent and severe hypertension than other NSAIDs and other selective COX-2 inhibitors. Therefore special attention should be paid to blood pressure monitoring during treatment with ECOXAR. If blood pressure rises significantly, alternative treatment should be considered.

Reported clinical studies suggest that the selective COX-2 inhibitor class of medicines such as etoricoxib, are associated with an increased risk of thrombotic events [especially myocardial infraction (MI) and stroke]. As the cardiovascular risks of selective COX-2 inhibitors such as etoricoxib as contained in ECOXAR may increase with dose and duration of exposure, the shortest duration possible and the lowest effective daily dose should be used. The patient's 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) should only be treated with ECOXAR after careful consideration.

ECOXAR is not a substitute for aspirin for cardiovascular prophylaxis because of its lack of effect on platelets. Because ECOXAR does not inhibit platelet aggregation, anti-platelet therapies should not be discontinued and if indicated, should be considered in patients at risk for or with a history of cardiovascular or other thrombotic events. There is no evidence that concurrent use of aspirin mitigates the increased risk of serious cardiovascular thrombotic events associated with ECOXAR. For more details, refer to section on interactions (section 4.5).

Serious skin reactions, some of them fatal, including exfoliative dermatitis, Stevens-Johnson syndrome, and toxic epidermal necrolysis, have been reported in association with the use of selective COX-2 inhibitors such as etoricoxib during post-marketing surveillance. Serious hypersensitivity reactions (such as anaphylaxis and angioedema) have been reported in patients receiving etoricoxib (see section 4.8).

Selective COX-2 inhibitors, such as ECOXAR have been associated with an increased risk of skin reactions in patients with a history of any allergy. ECOXAR should be discontinued at the first appearance of skin rash, mucosal lesions or any other sign of hypersensitivity.

When using ECOXAR in the elderly and in patients with renal, hepatic or cardiac dysfunction, medically appropriate supervision should be intensified. If these patients show deterioration during treatment, appropriate measures should be taken, including discontinuation of ECOXAR.

Gastrointestinal effects

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 at risk of developing a gastrointestinal complication with ECOXAR; the elderly, patients using any other NSAIDs or aspirin (acetylsalicylic acid)

concomitantly or patients with a prior history of gastrointestinal disease, such as perforation, ulceration and gastrointestinal bleeding.

There is an increase in risk of gastrointestinal adverse effects (gastrointestinal ulceration or other gastrointestinal complications) when ECOXAR is taken concomitantly with aspirin (even at low doses).

Elevations of alanine aminotransferase (ALT) and/or aspartate aminotransferase (AST) (approximately 3 or more times the upper limit of normal) have been reported in approximately 1 % of patients in clinical trials, treated for up to 1 year with etoricoxib 60 mg and 90 mg daily.

Any 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 (3 times the upper limit of normal) are detected, ECOXAR should be discontinued.

ECOXAR may mask fever and other signs of inflammation or infection.

Due to inhibition of prostaglandin synthesis, fluid retention and oedema have been reported in patients taking etoricoxib as contained in ECOXAR; therefore ECOXAR should be used with caution in patients with compromised cardiac function, and other conditions predisposing to or worsened by fluid retention. Patients with pre-existing congestive heart failure or hypertension should be closely monitored. All non-steroidal anti-inflammatory drugs (NSAIDs), including ECOXAR, can be associated with new onset or recurrent congestive heart failure (see section 4.8).

The use of ECOXAR is not recommended in fertile women attempting to conceive.

Neonatal renal impairment and Oligohydramnios:

The use of nonsteroidal anti-inflammatory drugs (NSAIDs) such as ECOXAR around 20 weeks gestation or later in pregnancy may cause fetal renal dysfunction leading to oligohydramnios and, in some cases, neonatal renal impairment. Complications of prolonged oligohydramnios may include limb contractures and delayed lung maturation. In some reported postmarketing cases of impaired neonatal renal function, invasive procedures such as exchange transfusion or dialysis were required. If NSAID treatment is determined necessary, limit use to the lowest effective dose and shortest duration possible. Avoid prescribing NSAIDs at 20 weeks and later in pregnancy because of the additional risk of premature closure of the fetal ductus arteriosus. Consider ultrasound monitoring of amniotic fluid if NSAID treatment extends beyond 48 hours. Discontinue the NSAID if oligohydramnios occurs (see section 4.3 and 4.6).

Drug Reaction with Eosinophillia and Systemic Symptoms (DRESS) has been reported in patients taking NSAIDs such as ECOXAR. Some of these events have been fatal or life-threatening. DRESS typically, although not exclusively, presents with fever, rash, lymphadenopathy, and/or facial swelling. Other clinical manifestations may include hepatitis, nephritis, haematological abnormalities, myocarditis, or myositis. Sometimes symptoms of DRESS may resemble an acute viral infection. Eosinophillia is often present. Because this disorder is variable in its presentation, other organ systems not noted here may be involved. It is important to note that early manifestations of hypersensitivity, such as fever or lymphadenopathy, may be present even though rash is not evident. If such signs or symptoms are present, discontinue ECOXAR and evaluate the patient immediately.

Lactose:

ECOXAR 30, 60, 90 and 90 mg tablets contain 1,05 ; 2,10; 3,15 and 4,20 mg lactose, respectively. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take ECOXAR.

4.5 Interaction with other medicines and other forms of interaction

Ciclosporin and tacrolimus: Co-administration of ciclosporin or tacrolimus with any NSAID, including ECOXAR, may increase the nephrotoxic effect of ciclosporin or tacrolimus. Renal function should be monitored when ECOXAR and either of these medicines is used in combination.

Warfarin: In subjects stabilised on chronic warfarin therapy, the administration of etoricoxib 120 mg daily was associated with an approximate 13 % increase in prothrombin time International Normalised Ratio (INR). Standard monitoring of INR values should be conducted when therapy with ECOXAR is initiated or changed in patients receiving warfarin or similar medicines.

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

Methotrexate: Two reported studies investigated the effects of etoricoxib 60 mg, 90 mg or 120 mg administered once daily for 7 days, in patients receiving once-weekly methotrexate doses of 7,5 mg to 20 mg for rheumatoid arthritis. Etoricoxib at 60 mg and 90 mg had no effect on methotrexate plasma concentrations (as measured by AUC) or renal clearance. In one reported study, etoricoxib 120 mg had no effect on methotrexate plasma concentrations (as measured by AUC) or renal clearance. In the other study, etoricoxib 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 ECOXAR at doses > 90 mg daily and methotrexate are administered concomitantly.

Diuretics, Angiotensin Converting Enzyme (ACE) Inhibitors and Angiotensin Receptor Blockers (ARBs): Reports suggest that non-selective NSAIDs and COX-2 selective inhibitors such as etoricoxib, as contained in ECOXAR may diminish the antihypertensive effect of diuretics, ACE inhibitors and Angiotensin Receptor Blockers (ARBs). This interaction should be given consideration in patients taking ECOXAR concomitantly with these medicines.

In 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 ECOXAR, the co-administration of ACE inhibitors or ARBs may result in a further deterioration of renal function, including possible acute renal failure. These effects may be reversible. Therefore, the combination should be administered with caution, especially in the elderly and in patients with impaired renal function. Patients should be adequately hydrated and consideration should be given to monitoring of renal function after initiation of concomitant therapy, and periodically thereafter.

Lithium: ECOXAR may increase plasma lithium levels. This interaction should be given consideration in patients taking ECOXAR concomitantly with lithium.

Aspirin: In a reported study in healthy subjects, at steady state, etoricoxib 120 mg once daily had no effect on the anti-platelet activity of aspirin (81 mg once daily). ECOXAR may be used concomitantly with aspirin at doses used for cardiovascular prophylaxis (low-dose aspirin). However, concomitant administration of low-dose aspirin with ECOXAR increases the rate of gastrointestinal ulceration, and other complications compared to use of etoricoxib alone. Concomitant administration of ECOXAR with doses of aspirin above those for cardiovascular prophylaxis or with other NSAIDs should be avoided (see section 4.4).
Concurrent use of aspirin does not mitigate the increased risk of serious cardiovascular thrombotic events associated with ECOXAR.

Oral Contraceptives: Etoricoxib 60 mg given concomitantly with an oral contraceptive containing 35 µg ethinyl estradiol (EE) and 0,5 mg to 1 mg norethindrone (NET) for 21 days, increased the steady state AUC_{0-24h} of EE by 37 %. Etoricoxib 120 mg given with the same oral contraceptive concomitantly or separated by 12 hours, increased the steady state AUC_{0-24h} of EE by 50 % to 60 %; however, (NET) concentrations generally did not increase to a clinically relevant degree. This increase in EE concentration should be considered when selecting an appropriate oral contraceptive for use with ECOXAR. An increase in EE exposure can increase the incidence of adverse events associated with oral contraceptives (e.g. venous thromboembolic events in women at risk).

Furosemide: Reported clinical studies have shown that NSAIDs such as etoricoxib, as contained in ECOXAR reduce the natriuretic and antihypertensive effect of furosemide and thiazides in patients. This response has been attributed to inhibition of renal prostaglandin synthesis.

Hormone Replacement Therapy: Administration of etoricoxib 120 mg with hormone replacement therapy consisting of conjugated oestrogens (0,625 mg conjugated oestrogens for 28 days, increased the mean steady state AUC_{0-24h} of unconjugated oestrone (41 %), equilin (76 %) and 17-beta-estradiol (22 %). The effect of the recommended chronic doses of etoricoxib (60 mg and 90 mg) has not been studied. The effects of etoricoxib 120 mg on the exposure (AUC_{0-24h}) to these oestrogenic components of conjugated oestrogens were less than half of those observed, when conjugated oestrogens was administered alone, and the dose was increased from 0,625 mg to 1,25 mg. The clinical significance of these increases is unknown, and higher doses of conjugated oestrogens were not studied in combination with etoricoxib. These increases in oestrogenic concentration should be taken into consideration when selecting postmenopausal hormone therapy for use with ECOXAR, because the increase in oestrogen

exposure might increase the risk of adverse events associated with Hormone Replacement Therapy (HRT).

Effects of etoricoxib on medicines metabolised by sulfotransferases: Etoricoxib is an inhibitor of human sulfotransferase activity, particularly SULT1E1, and has been shown to increase the serum concentrations of ethinyl oestradiol. While knowledge about effects of multiple sulfotransferases is presently limited and the clinical consequences for many medicines are still being examined, it may be prudent to exercise care when administering ECOXAR concurrently with other medicines primarily metabolised by human sulfotransferases (e.g. oral salbutamol and minoxidil).

Etoricoxib 120 mg once daily for 10 days in healthy volunteers did not alter the steady state plasma $AUC_{0\text{-}24h}$ or renal elimination of digoxin. There was an increase in digoxin C_{max} (approximately 33 %) (See section 4.3).

Other: In interaction studies, etoricoxib did not have clinically significant effects on the pharmacokinetics of prednisone/prednisolone.

Antacids do not have clinically significant effects on the pharmacokinetics of ECOXAR.

Ketoconazole, a potent inhibitor of CYP3A4, dosed at 400 mg once a day for 11 days to healthy volunteers did not have any clinically important effect on the single-dose pharmacokinetics of 60 mg etoricoxib (43 % increase in AUC).

4.6 Fertility, pregnancy and lactation

ECOXAR is contraindicated in pregnancy and lactation (see section 4.3)

Pregnancy

ECOXAR, as in other medicines inhibiting prostaglandin synthesis may cause uterine inertia and premature ductus arteriosis during the last trimester of pregnancy.

Pregnant women should not use ECOXAR at 20 weeks or later unless specifically advised to do so by health care professional because these medicines may cause foetal renal dysfunction (see section 4.3 and 4.4).

Breastfeeding:

Mothers on ECOXAR should not breastfeed their infants.

Fertility:

The use of ECOXAR is not recommended in fertile women attempting to conceive.

4.7 Effects on ability to drive and use machines

Patients who experience dizziness, vertigo or somnolence while taking ECOXAR should refrain from driving or operating machinery.

4.8 Undesirable effects

a) Summary of the safety profile

The following serious undesirable effects have been reported in association with the use of NSAIDs and cannot be ruled out for etoricoxib: nephrotoxicity including interstitial nephritis and nephrotic syndrome; hepatotoxicity including hepatic failure, and pancreatitis. In clinical studies, a higher incidence of adverse experiences was seen in older patients compared to younger patients.

b) Tabulated summary of adverse reactions

System organ class (SOC)	**Frequency**	**Adverse reaction**
Infections and infestations	Frequent Less frequent	Alveolar osteitis Gastroenteritis, upper respiratory infection, urinary tract infection
Blood and lymphatic system disorders	Less frequent Frequency unknown	Anaemia, leukopenia Thrombocytopenia
Immune system disorders	Frequency unknown	Hypersensitivity reactions, including angioedema, anaphylactic/anaphylactoid reactions including shock
Metabolism and nutrition disorders	Frequent Less frequent	Oedema/fluid retention Appetite increase or decrease, weight gain
Psychiatric disorders	Less frequent Frequency unknown	Anxiety, depression, mental acuity decreased Confusion, hallucinations, depression, restlessness
Nervous system disorders	Frequent Less frequent	Dizziness, headache Insomnia, paraesthesia/ hypaesthesia

	Frequency unknown	Dysgeusia, somnolence
Eye disorders	Less frequent Frequency unknown	Conjunctivitis Blurred vision
Ear and labyrinth disorders	Less frequent	Tinnitus, vertigo
Cardiac disorders	Frequent Less frequent Frequency unknown	Palpitations Atrial fibrillation, congestive heart failure, non-specific EGG changes, myocardial infarction, angina Aggravated hypertension, dysrhythmia cardiovascular thrombotic events and tachycardia
Vascular disorders	Frequent Less frequent Frequency unknown	Hypertension Flushing, cerebrovascular incidents (stroke), transient ischaemic attack, vasculitis Hypertensive crisis, peripheral oedema, aggravated hypertension

Respiratory, thoracic and mediastinal disorders	Less frequent Frequency unknown	Cough, dyspnoea, epistaxis Bronchospasm
Gastrointestinal disorders	Frequent Less frequent Frequency unknown	Gastrointestinal disorders (e.g. abdominal pain, flatulence, heartburn), diarrhoea, dyspepsia, epigastric discomfort, nausea Abdominal distension, acid reflux, bowel movement pattern change, constipation, dry mouth, gastroduodenal ulcer, irritable bowel syndrome, oesophagitis, oral ulcer, vomiting, gastritis, pancreatitis Peptic ulcers including gastro-intestinal perforation and bleeding (mainly in the elderly)
Hepato-biliary disorders	Frequent Frequency unknown	Increased ALT and AST Hepatitis, jaundice, hepatic failure
Skin and subcutaneous tissue disorders	Frequent Less frequent	Ecchymosis Facial oedema, pruritus, rash, erythema

	Frequency unknown	Urticaria, Stevens Johnson syndrome, toxic epidermal necrolysis, fixed drug eruption, Drug Reaction with Eosinophillia and Systemic Symptoms (DRESS) [see Warnings and Precautions]
Musculoskeletal, connective tissue and bone disorders	Less frequent	Muscular cramp/spasm, musculoskeletal pain/stiffness
Renal and urinary disorders	Less frequent Frequency unknown	Proteinuria, increased serum creatinine Renal insufficiency, including renal failure (see section 5.2) nephrotoxicity including interstitial nephritis and nephrotic syndrome
General disorders and administration site conditions	Frequent Less frequent	Asthenia/fatigue, flu like disease Chest pain
Investigations	Less frequent	Increased blood urea, increased creatine phosphokinase, decreased haematocrit, decreased haemoglobin, hyperkalaemia, decreased leukocytes, decreased platelets, increased uric acid, decreased blood sodium.

c) Description of selected adverse reactions

ECOXAR may cause fetal renal dysfunction leading to oligohydramnios and, in some cases, neonatal renal impairment. These adverse outcomes are reported, on average, after days to weeks of treatment, although oligohydramnios has been infrequently reported as soon as 48 hours after NSAID initiation. Oligohydramnios is often, but not always, reversible with treatment discontinuation (see section 4.3 and 4.4).

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care provders are asked to report any suspected adverse reactions to SAHPRA via the “6.04 Adverse Drug Reactions Reporting Form”, found online under SAHPRA’s publications:

https://www.sahpra.org.za/Publications/Index/8

4.9 Overdose

The most frequently observed adverse experiences were 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 dialysable by haemodialysis; it is not known whether etoricoxib is dialysable by peritoneal dialysis.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

A.3.1 Anti-Rheumatics (Anti-inflammatory Agents). ATC code: M01 AH05

Etoricoxib is a non-steroidal anti-inflammatory drug (NSAID) that exhibits anti-inflammatory, analgesic and antipyretic activities in animal models. Etoricoxib is an orally active, selective cyclo-oxygenase-2 (COX-2) inhibitor.

5.2 Pharmacokinetic properties

Absorption

Orally administered etoricoxib is absorbed with a mean oral bioavailability of approximately 100 %. Following 120 mg once-daily dosing to steady state, the peak plasma concentration (geometric mean C_{max}=3,6 µg/mL) was observed at approximately 1 hour (T_{max}) after administration to fasted adults. The geometric mean AUC_{0-24h} was 37,8 µg/h/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 reported clinical trials, etoricoxib was administered without regard to food.

The pharmacokinetics of etoricoxib in 12 healthy subjects (40 to 65 years of age) were similar (comparable AUC, C_{max} within approximately 20 %) when administered alone or with a magnesium/aluminium hydroxide antacid or a calcium carbonate antacid (approximately 50 mEq acid-neutralising capacity).

Distribution

In humans, etoricoxib is approximately 92 % bound to plasma protein over the range of concentrations of 0,05 µg/mL to 5 µg/mL. The volume of distribution at steady state (V_{dss}) is approximately 120 litre. Etoricoxib crosses the placenta and the blood-brain barrier.

Metabolism

Etoricoxib is extensively metabolised in the liver with <1 % of a dose recovered in urine as the parent drug. The major route of metabolism to form the 6'-hydroxymethyl derivative is catalysed 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.

Elimination

Following administration of a single 25 mg radio-labelled intravenous dose of etoricoxib to healthy subjects, 70 % of radioactivity was recovered in urine and 20 % in faeces, mostly as metabolites. Plasma and urine were collected for 7 days and stool collected for 10 days post-dose. 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 7 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.

Elderly

Pharmacokinetics in the elderly (65 years of age and older) with normal renal function are similar to those in the young. In reported clinical studies, a higher incidence of adverse experiences was seen in older patients compared to younger patients (see section 4.2).

Hepatic Insufficiency

Patients with mild hepatic insufficiency (Child-Pugh score 5 to 6) administered etoricoxib 60 mg once daily (for 21 days), 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 to 9) administered etoricoxib 60 mg every other day (for 21 days), had similar mean AUC to the healthy subjects given etoricoxib 60 mg once daily. There are no available clinical or pharmacokinetic data in patients with severe hepatic insufficiency (Child-Pugh score > 9) [see section 4.2 & 4.3]

Renal Insufficiency

The pharmacokinetics of a single dose of etoricoxib 120 mg in patients with moderate (creatinine clearance 30 to 50 mL/min) to severe (creatinine clearance of < 30 mL/min) renal insufficiency, and patients with end-stage renal disease on haemodialysis, were not significantly different from those in healthy subjects. Haemodialysis contributed negligibly to elimination (dialysis clearance approximately 50 mL/min).

Paediatric Population

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

In a pharmacokinetic study (N=16) reported in adolescents (aged 12 to 17) the pharmacokinetics in adolescents weighing 40 kg 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 efficacy of etoricoxib in paediatric and adolescent patients have not been established (see section 4.3).

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

- Cellulose microcrystalline
- calcium hydrogen phosphate anhydrous
- croscarmellose sodium
- magnesium stearate

Coating:

30 mg: Opadry II green 32K510020 (lactose monohydrate, hypromellose, titanium dioxide, triacetin, indigo carmine aluminium lake, iron oxide yellow)

60 mg: Opadry II green 35K510000 (lactose monohydrate, hypromellose, titanium dioxide, triacetin, indigo carmine aluminium lake, iron oxide yellow)

90 mg: Opadry II white 35K580003 (lactose monohydrate, hypromellose, titanium dioxide, triacetin)

120 mg: Opadry II green 32K510018 (lactose monohydrate, hypromellose, titanium dioxide, triacetin, indigo carmine aluminium lake, iron oxide yellow)

6.2 Incompatibilities

Not applicable

6.3 Shelf life

36 months

Store at or below 25 °C.

6.4 Special precautions for storage

Protect from moisture. Keep blister in carton until required for use.

6.5 Nature and contents of container

The tablets are packed in cold form blisters. Each blister strip contains

7 tablets. Carton contains 7 or 28 tablets.

Cold form blister pack

Cold form blister pack comprises of cold form blister laminate composed of oriented polyamide, aluminium foil and PVC film with backing of hard tempered aluminium foil coated with heat seal lacquer on the inner side.

7 HOLDER OF THE CERTIFICATE OF REGISTRATION

Ranbaxy Pharmaceuticals (Pty) Ltd

14 Lautre Road, Stormill, Ext.1,

Roodepoort, 1724

South Africa

8 REGISTRATION NUMBERS

ECOXAR 30 mg: 51/3.1/1144

ECOXAR 60 mg: 51/3.1/1145

ECOXAR 90 mg: 51/3.1/1146

ECOXAR 120 mg: 51/3.1/1147

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of registration: February 2020

Marketed by Unicorn Pharmaceuticals (Pty) Ltd

10 DATE OF REVISION OF THE TEXT

21 January 2022

* ECOXAR 30 mg is not marketed, another etoricoxib 30 mg brand can be used for this dose.

PROFESSIONELE INLIGTING

SKEDULERINGSTATUS

S3

1. NAAM VAN DIE MEDISYNE

ECOXAR 30 mg Filmbedekte tablette

ECOXAR 60 mg Filmbedekte tablette

ECOXAR 90 mg Filmbedekte tablette

ECOXAR 120 mg Filmbedekte tablette

2. KWALITATIEWE EN KWANTITATIEWE SAMESTELLING

ECOXAR 30 mg

Elke filmbedekte tablet bevat 30 mg etorikoksib.

Bevat suiker: 1,05 mg laktosemonohidraat/filmbedekte tablet.

ECOXAR 60 mg

Elke filmbedekte tablet bevat 60 mg etorikoksib.

Bevat suiker: 2,10 mg laktosemonohidraat/filmbedekte tablet.

ECOXAR 90 mg

Elke filmbedekte tablet bevat 90 mg etorikoksib.

Bevat suiker: 3,15 mg laktosemonohidraat/filmbedekte tablet.

ECOXAR 120 mg

Elke filmbedekte tablet bevat 120 mg etorikoksib.

Bevat suiker: 4,20 mg laktosemonohidraat/filmbedekte tablet.

Vir die volledige lys van hulpstowwe, sien afdeling 6.1.

3. FARMASEUTIESE VORM

ECOXAR 30 mg

Blougroen, filmbedekte, ronde, bikonvekse tablette, met E30 aan die een kant ingepers en skoon aan die ander kant.

ECOXAR 60 mg

Groen tot donkergroen, filmbedekte, ronde, bikonvekse tablette, met E60 aan die een kant ingepers en skoon aan die ander kant.

ECOXAR 90 mg

Wit tot naaswit, filmbedekte, ronde, bikonvekse tablette, met E90 aan die een kant ingepers en skoon aan die ander kant.

ECOXAR 120 mg

Liggroen tot dowwe groen, filmbedekte, ronde, bikonvekse tablette, met E120 aan die een kant ingepers en skoon aan die ander kant.

4 KLINIESE BESONDERHEDE

4.1 Terapeutiese indikasies

ECOXAR word aangedui vir:

- simptomatiese verligting van osteoartritis (OA) en rumatoïede artritis (RA).
- behandeling van ankiloserende spondilitis (AS).
- behandeling van akute jigartritis.
- korttermynverligting van akute pyn, behandeling beperk tot ’n maksimum tydperk van 8 dae.
- behandeling van primêre dismenorree.
- behandeling van matige tot ernstige akute postoperatiewe pyn geassosieer met tandheelkundige chirurgie.

Die besluit om ’n selektiewe COX-2-inhibeerder voor te skryf, moet gebaseer wees op ’n evaluering van die individuele pasiënt se risiko's in die geheel (sien afdeling 4.4).

4.2 Posologie en metode van toediening

Posologie

ECOXAR word oraal toegedien. ECOXAR kan met of sonder voedsel geneem word. ECOXAR moet vir die kortste moontlike tydperk en teen die laagste daaglikse dosis wat effektief is, gebruik word.

Osteoartritis (OA): Die aanbevole dosis is 30 mg* een keer per dag. By sommige pasiënte wat onvoldoende verligting van simptome ervaar, kan die dosis tot 60 mg een keer per dag verhoog word.

Rumatoïede artritis (RA): Die aanbevole dosis is 90 mg een keer per dag. By sommige pasiënte, kan 60 mg een keer dag voldoende terapeutiese voordeel bied.

Ankiloserende spondilitis: Die aanbevole dosis is 90 mg een keer per dag. By sommige pasiënte, kan 60 mg een keer per dag voldoende terapeutiese voordeel bied.

Korttermynverligting van akute pyn: Die aanbevole dosis is 90 mg of 120 mg een keer per dag, beperk tot ’n maksimum behandelingstydperk van 8 dae.

Akute jigagtige artritis: Die aanbevole dosis is 120 mg een keer per dag, beperk tot ’n maksimum behandelingstydperk van 8 dae.

Primêre dismenorree: Die aanbevole dosis is 120 mg een keer per dag.

Postoperatiewe tandheelkundige pyn: Die aanbevole dosis is 90 mg een keer per dag.

Dosisse hoër as die wat aanbeveel word vir elke indikasie het óf nie bykomende doeltreffendheid gedemonstreer nie óf is nie bestudeer nie.

Daarom:

Moet die dosis vir OA nie 60 mg daagliks oorskry nie.

Moet die dosis vir RA nie 90 mg daagliks oorskry nie.

Moet die dosis vir ankiloserende spondilitis nie 90 mg daagliks oorskry nie.

Moet die dosis vir akute jig nie 120 mg daagliks oorskry nie.

Moet die dosis vir akute pyn en primêre dismenorree nie 120 mg daagliks oorskry nie.

Moet die dosis vir postoperatiewe akute pyn na tandheelkundige chirurgie nie 90 mg daagliks oorskry nie.

Omdat die kardiovaskulêre risiko’s van ECOXAR kan verhoog met dosis en duur van blootstelling, moet die kortste moontlike duur en die laagste effektiewe daaglikse dosis gebruik word. Die pasiënt se behoefte aan simptomatiese verligting en respons op terapie moet periodiek herevalueer word (sien afdeling 4.4).

Spesiale populasies

Bejaardes

Geen dosisaanpassing vir ECOXAR is nodig by bejaardes nie. Bejaarde pasiënte kan egter meer vatbaar vir renale, gastroïntestinale en kardiovaskulêre newe-effekte wees (sien afdeling 4.4).

Wanneer ECOXAR by bejaardes en by pasiënte met renale, hepatiese of kardiale wanfunksie gebruik word, moet toepaslike mediese toesig versterk word.

Indien hierdie pasiënte agteruitgang toon tydens behandeling, moet toepaslike maatreëls ingestel word, insluitende staking van ECOXAR.

Hepatiese belemmering

By pasiënte met geringe lewerinkorting (Child-Pughtelling 5 tot 6), moet ’n dosis van 60 mg een keer per dag nie oorskry word nie.

By pasiënte met matige lewerinkorting (Child-Pughtelling 7 tot 9), moet die dosis verminder word; ’n dosis van 60 mg elke tweede dag moet nie oorskry word nie, toediening van ECOXAR 30 mg* een keer per dag kan ook oorweeg word.

Kliniese ervaring is beperk, veral by pasiënte met matige lewerdisfunksie. Daar is geen kliniese of farmakokinetiese data by pasiënte met erge lewerinkorting (Child-Pughtelling > 9) nie, daarom word die gebruik van ECOXAR teenaangedui by hierdie pasiënte (sien afdelings 4.3 en 5.2).

Renale belemmering

Geen dosisaanpassing is nodig vir pasiënte met ligter grade van nierinkorting (kreatinienopruiming ≥ 30 mL/min) nie. Die gebruik van ECOXAR by pasiënte met kreatinienopruiming < 30 mL/min word teenaangedui (sien afdeling 4.3).

Wanneer ECOXAR by bejaardes en by pasiënte met renale, hepatiese of kardiale wanfunksie gebruik word, is strenger toepaslike mediese toesig nodig. Indien pasiënte tydens behandeling agteruitgang toon, moet toepaslike maatreëls ingestel word, insluitende staking van ECOXAR.

4.3 Kontra-indikasies

ECOXAR word teenaangedui by:

- pasiënte met bekende hipersensitiwiteit vir enige van die hulpmiddels in ECOXAR (sien afdeling 6.1)
- pasiënte met aktiewe peptiese ulkusse of gastroïntestinale (GI) bloeding
- pasiënte met erge lewerdisfunksie (Child-Pughtelling > 9 of serumalbumien < 25 g/liter)
- pasiënte met beraamde kreatinienopruiming < 30 mL/min
- pasiënte wat tekens van asma, akute rinitis, poliepe in die neus, angio-edeem of urtikarie ontwikkel het na toediening van aspirien of ander niesteroïdale antiinflammatoriese geneesmiddels (NSAIM's) insluitende etorikoksib, soos bevat in ECOXAR
- ongekontroleerde hipertensie
- swangerskap en borsvoeding, vermy dit om NSAIM's soos ECOXAR na 20 weke voor te skryf, aangesien dit in seldsame gevalle nierprobleme by ongebore babas kan veroorsaak (sien afdeling 4.4)
- kinders en adolessente jonger as 16 jaar
- pasiënte met inflammatoriese dermsiekte
- pasiënte met kongestiewe hartversaking (NYHA II – IV)
- bevestigde iskemiese hartsiekte, perifere arteriële siekte en/of serebrovaskulêre siekte (sien afdeling 4.4)
- peri-operatiewe analgesie in die opset van koronêre arterie omleidingsoperasie
- litiumterapie – gepaardgaande toediening met ECOXAR mag tot toksiese bloedvlakke van litium lei (sien afdeling 4.5)
- digoksien – daar was ’n toename van ongeveer 33 % in die C_{maks} van digoksien by gesonde vrywilligers (sien afdeling 4.5).

4.4 Spesiale waarskuwings en voorsorgmaatreëls vir gebruik

ECOXAR mag die pasiënt vatbaar maak vir kardiovaskulêre voorvalle, gastroïntestinale effekte of kutane reaksies, wat noodlottig kan wees.

Kliniese proewe dui daarop dat die selektiewe COX-2-inhibeerder klas van medisyne, soos ECOXAR, gepaardgaan met ’n verhoogde risiko van arteriële trombotiese voorvalle (veral miokardiale infarksie [MI] en beroerte).

Langtermyntoediening van NSAIM's soos ECOXAR, het tot renale papillêre nekrose en ander nierskade gelei. Renale prostaglandiene kan ’n kompenserende rol in die handhawing van renale perfusie speel. Daarom, onder toestande van gekompromitteerde renale perfusie, kan toediening van ECOXAR ’n afname in die vorming van prostaglandien en tweedens in renale bloedvloei veroorsaak, en sodoende nierfunksie verswak. Pasiënte wat die grootste risiko vir hierdie respons het, is diegene met voorafbestaande beduidende ingekorte nierfunksie, ongekompenseerde hartversaking of lewersirrose. Dit is nodig om nier- en lewerfunksie by sulke pasiënte te monitor.

Omsigtigheid is nodig wanneer behandeling met ECOXAR in pasiënte met dehidrasie geïnisieer word. Dit is raadsaam om pasiënte te rehidreer voordat terapie met ECOXAR begin word.

Vloeistofretensie, edeem en hipertensie is waargeneem by pasiënte wat ECOXAR gebruik. Alle niesteroïdale antiinflammatoriese geneesmiddels (NSAIM's), insluitende ECOXAR, kan met nuwe aanvang of herhaalde kongestiewe hartversaking geassosieer word. Sorg moet uitgeoefen word by pasiënte met ’n geskiedenis van hartversaking, linkerventrikulêre disfunksie of hipertensie, en by pasiënte met voorafbestaande edeem om enige ander rede. Indien daar kliniese bewyse is van agteruitgang in die toestand van hierdie pasiënte, moet toepaslike maatreëls, insluitende staking van ECOXAR, getref word.

ECOXAR mag met meer gereelde en erge hipertensie vergeleke met ander NSAIM's en ander selektiewe COX-2-inhibeerders gepaardgaan. Daarom moet spesiale aandag aan monitering van bloeddruk tydens behandeling met ECOXAR gegee word. Indien die bloeddruk aansienlik styg, moet alternatiewe behandeling oorweeg word.

Gerapporteerde kliniese proewe stel voor dat die selektiewe COX-2-inhibeerder klas van medisyne, soos etorikoksib, gepaardgaan met ’n hoër risiko van trombotiese voorvalle (veral miokardiale infarksie [MI] en beroerte). Aangesien die kardiovaskulêre risiko’s van selektiewe COX-2-inhibeerders soos etorikoksib, soos bevat in ECOXAR, met dosis en duur van blootstelling mag toeneem, moet die korste moontlike duur en die laagste doeltreffende daaglikse dosis gebruik

word. Die pasiënt se behoefte vir simptomatiese verligting en respons op terapie moet periodiek herevalueer word.

Pasiënte met beduidende risikofaktore vir kardiovaskulêre voorvalle (bv. hipertensie, hiperlipidemie, diabetes mellitus, rook) moet slegs na sorgvuldige oorweging met ECOXAR behandel word.

ECOXAR is nie ’n plaasvervanger vir aspirien vir kardiovaskulêre profilakse nie vanweë die gebrek aan effek op plaatjies. Aangesien ECOXAR nie plaatjieklomping onderdruk nie, moet antiplaatjieterapieë nie gestaak word nie, en indien aangedui, moet dit oorweeg word by pasiënte met ’n risiko vir of ’n geskiedenis van kardiovaskulêre of ander trombotiese voorvalle. Daar is geen bewyse dat gelyktydige gebruik van aspirien die verhoogde risiko vir ernstige kardiovaskulêre trombotiese voorvalle, geassosieer met ECOXAR, verlaag nie. Vir meer besonderhede, verwys na afdeling oor interaksies (afdeling 4.5).

Ernstige velreaksies, waarvan sommige dodelik was, insluitende afskilferende dermatitis, Stevens-Johnson-sindroom, en toksiese epidermale nekrolise, is tydens nabemarkingsopnames gepaardgaande met die gebruik van selektiewe COX-2-inhibeerders, soos etorikoksib, gerapporteer. Ernstige hipersensitiwiteitsreaksies (soos anafilakse en angio-edeem) is gerapporteer by pasiënte wat etorikoksib ontvang het (sien afdeling 4.8).

Selektiewe COX-2-inhibeerders, soos in ECOXAR, is geassosieer met ’n hoër risiko van velreaksies by pasiënte met ’n geskiedenis van enige allergie. ECOXAR moet gestaak word met die eerste tekens van veluitslag, letsels aan slymvliese of enige ander teken van hipersensitiwiteit.

Wanneer ECOXAR gebruik word by bejaardes en by pasiënte met nier-, lewer- of hartdisfunksie, moet geskikte mediese toesig versterk word. Indien hierdie pasiënte tydens behandeling agteruitgaan, moet toepaslike maatreëls getref word, insluitende staking van ECOXAR.

Gastroïntestinale effekte

Komplikasies van die boonste gastroïntestinale weg (perforasies, ulkusse of bloedings [PUB's]), waarvan sommige ’n noodlottige uitkoms gehad het, het voorgekom in pasiënte wat met etorikoksib behandel is.

Wees versigtig wanneer pasiënte behandel word wat ’n risiko het om ’n gastroïntestinale komplikasie met ECOXAR te ontwikkel; bejaardes, pasiënte wat ander NSAIM's of aspirien (asetielsalisielsuur) terselfdertyd gebruik of pasiënte met ’n voorafgaande geskiedenis van gastroïntestinale siekte, soos perforasie, ulserasie en gastroïntestinale bloeding.

Daar is ’n verhoging in risiko vir gastroïntestinale nadelige effekte (gastroïntestinale ulserasie of ander gastroïntestinale komplikasies) wanneer ECOXAR saam met aspirien geneem word (selfs teen lae dosisse).

Verhoging van alanienaminotransferase (ALT) en/of aspartaataminotransferase (AST) (ongeveer 3 of meer keer die boonste grens van normaal) is gerapporteer by ongeveer 1 % van pasiënte in kliniese proewe wat met 60 mg of 90 mg etorikoksib daagliks vir tot 1 jaar behandel is.

Enige pasiënt met simptome en/of tekens aanduidend van lewerdisfunksie, of in wie ’n abnormale lewerfunksietoets voorgekom het, moet geëvalueer word vir aanhoudende abnormale lewerfunksietoetse. Indien aanhoudende abnormale lewerfunksietoetse (3 keer die boonste grens van normaal) opgemerk word, moet ECOXAR gestaak word.

ECOXAR kan koors en ander tekens van inflammasie of infeksie verberg.

Weens inhibisie van prostaglandiensintese, is vloeistofretensie en edeem waargeneem by pasiënte wat etorikoksib, soos bevat in ECOXAR, neem; daarom moet ECOXAR versigtig gebruik word by pasiënte met verswakte hartfunksie, en ander toestande wat vloeistofretensie kan aanbring of daardeur vererger kan word. Pasiënte met voorafbestaande kongestiewe hartversaking of hipertensie moet noukeurig gemonitor word. Alle niesteroïdale antiinflammatoriese geneesmiddels (NSAIM's), insluitende ECOXAR, kan met nuwe of herhaalde kongestiewe hartversaking gepaardgaan (sien afdeling 4.8).

Gebruik van ECOXAR word nie aanbeveel vir gebruik deur vrugbare vroue wat probeer om swanger te raak nie.

Neonatale renale belemmering en oligohidramnios:

Die gebruik van niesteroïdale antiinflammatoriese geneesmiddels (NSAIM's) soos ECOXAR rondom 20 weke gestasie of later in die swangerskap, mag renale disfunksie by die fetus veroorsaak wat tot oligohidramnios (amnionvloeistoftekort) en, in sommige gevalle, neonatale renale belemmering lei. Komplikasies van langdurige oligohidramnios mag kontrakture van die ledemate en vertraagde maturasie van die longe insluit. In sommige gerapporteerde nabemarkingsgevalle van belemmerde neonatale nierfunksie was ingrypende prosedures soos uitruiltransfusie of dialise nodig. Indien behandeling met ’n NSAIM noodsaaklik geag word, beperk gebruik tot die laagste effektiewe dosis en kortste moontlike duur. Vermy dit om NSAIM's teen 20 weke en later tydens swangerskap voor te skryf, weens die bykomende risiko van voortydige sluiting van die fetale ductus arteriosus. Oorweeg monitering van amnionvloeistof met behulp van ultraklank indien NSAIM-behandeling langer as 48 uur duur. Staak die NSAIM indien oligohidramnios voorkom (sien afdelings 4.3 en 4.6).

Geneesmiddelreaksie met eosinofilie en sistemiese simptome (DRESS) is aangemeld by pasiënte wat NSAIM's soos ECOXAR neem. Sommige van hierdie gebeure was noodlottig of lewensgevaarlik. DRESS vertoon tipies, hoewel nie uitsluitlik nie, met koors, uitslag, limfadenopatie en/of gesigswelling. Ander kliniese manifestasies kan hepatitis, nefritis, hematologiese abnormaliteite, miokarditis of miositis insluit. Soms kan simptome van DRESS soos 'n akute virusinfeksie lyk. Eosinofilie is dikwels teenwoordig. Omdat hierdie afwyking veranderlik is in sy voorkoms, kan ander orgaanstelsels wat nie hier genoem word nie, betrokke wees. Dit is belangrik om daarop te let dat vroeë manifestasies van hipersensitiwiteit, soos koors of limfadenopatie, teenwoordig kan wees al is die uitslag nie duidelik nie. Indien sulke tekens of simptome teenwoordig is, staak ECOXAR en evalueer die pasiënt onmiddellik.

Laktose:

ECOXAR 30, 60, 90 en 120 mg tablette bevat 1,05; 2,10; 3,15 en 4,20 mg laktose, onderskeidelik. Pasiënte met die seldsame oorerflike toestande van galaktose-intoleransie, algehele laktasegebrek of glukose-galaktose-wanabsorpsie behoort nie ECOXAR te neem nie.

4.5 Interaksie met ander medisyne en ander vorms van interaksie

Siklosporien en takrolimus: Gelyktydige toediening van siklosporien of takrolimus saam met enige NSAIM, insluitende ECOXAR, mag die nefrotoksiese effek van siklosporien of takrolimus versterk. Nierfunksie moet gemonitor word wanneer ECOXAR en enigeen van hierdie medisynes in kombinasie gebruik word.

Warfarien: In proefpersone wat op chroniese terapie met warfarien gestabiliseer is, het die toediening van 120 mg etorikoksib daagliks gepaardgegaan met ’n toename van ongeveer 13 % in protrombientyd / internasionale genormaliseerde verhouding (IGV). Standaard monitering van IGV-waardes moet uitgevoer word as terapie met ECOXAR begin of verander word by pasiënte wat warfarien of soortgelyke medisyne ontvang.

Rifampisien: Gelyktydige toediening van etorikoksib saam met rifampisien, ’n kragtige induseerder van hepatiese metabolisme, het ’n 65 % afname in area-onder-die-kurwe (AOK) van etorikoksib in die plasma veroorsaak. Hierdie interaksie moet in ag geneem word wanneer ECOXAR saam met rifampisien toegedien word.

Metotreksaat: Twee gerapporteerde studies het die effekte van 60 mg, 90 mg of 120 mg etorikoksib een keer per dag toegedien vir 7 dae aan pasiënte wat een keer per week metotreksaatdosisse van 7,5 mg tot 20 mg vir rumatoïede artritis ontvang het, ondersoek. Etorikoksib teen 60 mg en 90 mg het geen effek op metotreksaat plasmakonsentrasies (soos gemeet deur AOK) of nieropruiming gehad nie. In een gerapporteerde studie, het 120 mg etorikoksib geen effek op metotreksaat plasmakonsentrasies (soos gemeet deur AOK) of nieropruiming gehad nie. In die ander studie, het 120 mg etorikoksib die metotreksaat plasmakonsentrasies met 28 % verhoog (soos gemeet as AOK) en nieropruiming van metotreksaat

met 13 % verminder. Monitering vir metotreksaat-verwante toksisiteit moet oorweeg word wanneer ECOXAR teen dosisse >90 mg daagliks gepaardgaande met metotreksaat toegedien word.

Diuretika, angiotensienomsettingsensiem- (AOE-)inhibeerders en angiotensienreseptor-blokkeermiddels (ARB's): Verslae toon dat nieselektiewe NSAIM's en COX-2 selektiewe inhibeerders soos etorikoksib, soos bevat in ECOXAR**,** die antihipertensiewe effek van diuretika, AOE-inhibeerders en angiotensienreseptorblokkeermiddels (ARB's) kan verminder. Hierdie interaksie moet in aanmerking geneem word by pasiënte wat ECOXAR gepaardgaande met hierdie medisyne neem.

By pasiënte met ingekorte nierfunksie (bv. bejaarde pasiënte of pasiënte met volume-uitputting, insluitende dié op diuretiese terapie) wat met ECOXAR behandel word, kan die gelyktydige toediening van AOE-inhibeerders of ARB's ’n verdere agteruitgang in nierfunksie, waaronder moontlike akute nierversaking, veroorsaak. Hierdie effekte kan omkeerbaar wees. Daarom moet die kombinasie met omsigtigheid toegedien word, veral by bejaardes en by pasiënte met ingekorte nierfunksie. Pasiënte moet voldoende gehidreer wees en dit moet oorweeg word om nierfunksie na aanvang van die gesamentlike terapie, en periodiek daarna, te monitor.

Litium: ECOXAR mag vlakke van litium in die plasma verhoog. Hierdie interaksie moet in aanmerking geneem word by pasiënte wat ECOXAR saam met litium neem.

Aspirien: In ’n gerapporteerde studie met gesonde proefpersone, by ewewigsvlak, het 120 mg etorikoksib een keer per dag geen effek op die antiplaatjie-aktiwiteit van aspirien (81 mg een keer per dag) gehad nie. ECOXAR mag saam met aspirien gebruik word teen dosisse wat gebruik word vir kardiovaskulêre profilakse (lae-dosis aspirien). Gesamentlike toediening van lae-dosis aspirien met ECOXAR verhoog egter die voorkoms van gastroïntestinale ulserasie en ander komplikasies, vergeleke met die gebruik van etorikoksib alleen. Gepaardgaande toediening van ECOXAR met dosisse van aspirien hoër as dié vir kardiovaskulêre profilakse of met ander NSAIM's moet vermy word (sien afdeling 4.4).

Gesamentlike gebruik van aspirien verlig nie die verhoogde risiko van ernstige kardiovaskulêre trombotiese voorvalle geassosieer met ECOXAR nie.

Orale voorbehoedmiddels: 60 mg etorikoksib wat vir 21 dae toegedien is saam met ’n orale kontraseptiewe middel wat 35 µg etinielestradiol (EE) en 0,5 mg tot 1 mg noretindroon (NET) bevat, het die ewewigsvlak AOK_{0-24h} van EE met 37 % verhoog. 120 mg etorikoksib toegedien met dieselfde orale voorbehoedmiddel gelyktydig of 12 uur apart, het die ewewigsvlak AOK_{0-24h} van EE met 50 % tot 60 % verhoog; NET-konsentrasies het egter oor die algemeen nie tot ’n klinies relevante mate verhoog nie. Hierdie toename in EE-konsentrasie moet in gedagte gehou word wanneer ’n gepaste orale voorbehoedmiddel vir gebruik saam met ECOXAR gekies word. ’n Toename in EE-blootstelling kan die voorkoms van nadelige effekte vanweë orale voorbehoedmiddels (bv. veneuse trombo-emboliese voorvalle by vroue met risiko) verhoog.

Furosemied: Gerapporteerde kliniese studies het getoon dat NSAIM's soos etorikoksib, soos bevat in ECOXAR, die natriuretiese en antihipertensiewe effek van furosemied en tiasiede by pasiënte verminder. Hierdie respons word toegeskryf aan inhibisie van renale prostaglandiensintese.

Hormoonvervangingsterapie: Toediening van 120 mg etorikoksib saam met hormoonvervangingsterapie bestaande uit gekonjugeerde estrogene (0,625 mg gekonjugeerde estrogene) vir 28 dae, het die gemiddelde ewewigsvlak AOK_{0-24h} van ongekonjugeerde estroon (41 %), ekwilien (76 %) en 17-beta-estradiol (22 %) verhoog. Die effek van die aanbevole chroniese dosisse van etorikoksib (60 mg en 90 mg) is nie bestudeer nie. Die effek van 120 mg etorikoksib op die blootstelling (AOK_{0-24h}) aan hierdie estrogeniese komponente van gekonjugeerde estrogene was minder as die helfte van dié wat met gekonjugeerde estrogene alleen toegedien, waargeneem is en die dosis van 0,625 mg tot 1,25 mg verhoog is. Die kliniese betekenis van hierdie verhogings is onbekend en hoër dosisse van gekonjugeerde estrogene is nie in kombinasie met etorikoksib bestudeer nie. Hierdie verhogings in estrogeenkonsentrasie moet in aanmerking geneem word wanneer postmenopousale hormoonterapie vir gebruik saam met ECOXAR oorweeg word, omdat

die toename in estrogeenblootstelling die risiko van nadelige effekte geassosieer met hormoonvervangingsterapie (HVT) kan verhoog.

Effekte van etorikoksib op medisyne wat deur sulfotransferases gemetaboliseer word: Etorikoksib is ’n inhibeerder van menslike sulfotransferase aktiwiteit, veral SULT1E1, en daar is getoon dat dit die serumkonsentrasies van etinielestradiol verhoog. Terwyl kennis oor die effekte van vele sulfotransferases tans beperk is en die kliniese gevolge vir baie middels steeds ondersoek word, mag dit raadsaam wees om versigtig te wees wanneer ECOXAR gelyktydig met ander medisyne wat hoofsaaklik deur menslike sulfotransferases gemetaboliseer word, toegedien word (bv. orale salbutamol en minoksidiel).

120 mg etorikoksib een keer per dag vir 10 dae aan gesonde proefpersone het nie die ewewigsvlak plasma $AOK_{0\text{-}24h}$ of renale uitskeiding van digoksien verander nie. Daar was ’n toename in digoksien C_{maks} (ongeveer 33 %) (sien afdeling 4.3).

Ander: In interaksiestudies het etorikoksib nie klinies beduidende effekte op die farmakokinetika van prednisoon/prednisoloon gehad nie.

Teensuurmiddels het nie klinies betekenisvolle effekte op die farmakokinetika van ECOXAR nie.

Ketokonasool, ’n kragtige inhibeerder van CYP3A4, gedoseer teen 400 mg een keer per dag vir 11 dae aan gesonde proefpersone het geen klinies belangrike effek op die enkeldosis farmakokinetika van 60 mg etorikoksib gehad nie (43 % toename in AOK).

4.6 Vrugbaarheid, swangerskap en borsvoeding

ECOXAR word teenaangedui tydens swangerskap en borsvoeding (sien afdeling 4.3)

Swangerskap:

ECOXAR, soos by ander medisyne wat prostaglandiensintese inhibeer, kan baarmoederbeweginglоosheid en premature ductus arteriosus gedurende die laaste trimester van swangerskap veroorsaak

Swanger vroue moet nie ECOXAR gebruik indien hulle 20 weke of meer swanger is nie, behalwe indien ’n gesondheidsorgdeskundige dit spesifiek so geadviseer het, want hierdie medisyne kan renale disfunksie by die fetus veroorsaak (sien afdelings 4.3 en 4.4).

Borsvoeding:

Moeders wat ECOXAR gebruik, behoort nie hul babas te borsvoed nie.

Vrugbaarheid:

Die gebruik van ECOXAR word nie aanbeveel by vrugbare vrouens wat probeer om swanger te raak nie.

4.7 Uitwerking op die vermoë om te bestuur en masjiene te gebruik

Pasiënte wat duiseligheid, vertigo of slaperigheid ervaar terwyl hulle ECOXAR neem, moet dit vermy om te bestuur of masjinerie te hanteer.

4.8 Ongewenste effekte

a) Opsomming van die veiligheidsprofiel

Die volgende ernstige ongewenste effekte is gepaardgaande met die gebruik van NSAIM's gerapporteer en kan nie vir etorikoksib uitgesluit word nie: nefrotoksisiteit insluitende interstisiële nefritis en nefrotiese sindroom; hepatotoksisiteit insluitende lewerversaking, en pankreatitis. In kliniese studies is ’n hoër insidensie van ongunstige reaksies by ouer pasiënte in vergelyking met jonger pasiënte gesien.

b) Getabuleerde opsomming van ongunstige reaksies

Stelsel orgaan klas (SOK)	**Frekwensie**	**Ongunstige reaksie**
Infeksies en infestasies	Dikwels Minder dikwels	Alveolêre osteïtis Gastroënteritis, boonstelugweginfeksie, urienweginfeksie

Stelsel orgaan klas (SOK)	**Frekwensie**	**Ongunstige reaksie**
Bloed- en limfstelselversteurings	Minder dikwels Frekwensie onbekend	Anemie, leukopenie Trombositopenie
Immuunstelselversteurings	Frekwensie onbekend	Hipersensitiwiteitsreaksies, insluitende angio-edeem, anafilaktiese/anafilaktoïede reaksies insluitende skok
Metabolisme en voedingsversteurings	Dikwels Minder dikwels	Edeem/vloeistofretensie Toename of afname in eetlus, gewigstoename
Psigiatriese versteurings	Minder dikwels Frekwensie onbekend	Angstigheid, depressie, verminderde verstandelike skerpheid Verwardheid, hallusinasies, depressie, rusteloosheid
Senuweestelselversteurings	Dikwels Minder dikwels Frekwensie onbekend	Duiseligheid, hoofpyn Slaaploosheid, parestesie/hipestesie Disgeusie, slaperigheid
Oogversteurings	Minder dikwels Frekwensie onbekend	Konjunktivitis Versteurde visie
Oor- en labirintversteurings	Minder dikwels	Tinnitus, vertigo
Kardiale versteurings	Dikwels Minder dikwels	Hartkloppings Atriale fibrillasie, kongestiewe hartversaking, niespesifieke EKG-veranderings, miokardiale infarksie, angina

Stelsel orgaan klas (SOK)	**Frekwensie**	**Ongunstige reaksie**
	Frekwensie onbekend	Verergerde hipertensie, disritmie, kardiovaskulêre trombotiese voorvalle en tagikardie
Vaskulêre versteurings	Dikwels Minder dikwels Frekwensie onbekend	Hipertensie Blosing, serebrovaskulêre insidente (beroerte), vlietende iskemiese aanval, vaskulitis Hipertensiewe krisis, perifere edeem, verergerde hipertensie
Respiratoriese, torakale en mediastinale versteurings	Minder dikwels Frekwensie onbekend	Hoes, dispnee, epistakse Brongospasma
Gastroïntestinale versteurings	Dikwels Minder dikwels Frekwensie onbekend	Gastroïntestinale versteurings (bv. abdominale pyn, winderigheid, sooibrand), diarree, dispepsie, epigastriese ongemak, naarheid Abdominale opsetting, suurrefluks, verandering in die ontlastingpatroon, hardlywigheid, droë mond, gastroduodenale ulkus, prikkelbaredermsindroom, esofagitis, mondulkus, braking, gastritis, pankreatitis Peptiese ulkusse insluitende gastroïntestinale perforasie en bloeding (hoofsaaklik by bejaardes)
Hepatobiliêre versteurings	Dikwels	Verhoogde ALT en AST Hepatitis, geelsug, lewerversaking

Stelsel orgaan klas (SOK)	**Frekwensie**	**Ongunstige reaksie**
	Frekwensie onbekend	
Vel- en subkutane weefselversteurings	Dikwels Minder dikwels Frekwensie onbekend	Ekchimose Gesigsedeem, pruritus, uitslag, eriteem Urtikarie, Stevens-Johnson-sindroom, toksiese epidermale nekrolise, vaste middeluitslag. Geneesmiddelreaksie met Eosinophilia en Sistemiese Simptome (DRESS) (sien afdeling 4.4)
Muskuloskeletale, bindweefsel- en beenversteurings	Minder dikwels	Spierkrampe/spasmas, muskuloskeletale pyn/styfheid
Nier- en urienwegversteurings	Minder dikwels Frekwensie onbekend	Proteïnurie, verhoogde serumkreatinien Renale ontoereikendheid, insluitende nierversaking (sien afdeling 5.2), nefrotoksisiteit, insluitende interstisiële nefritis en nefrotiese sindroom
Algemene versteurings en toestande by die plek van toediening	Dikwels Minder dikwels	Astenie/moegheid, griepagtige siekte Pyn in die borskas
Ondersoeke	Minder dikwels	Verhoogde bloedureum, verhoogde kreatienfosfokinase, verlaagde hematokrit, verlaagde hemoglobien, hiperkalemie, verminderde leukosiete, verminderde plaatjies, verhoogde uriensuur, afname van natrium in die bloed.

c) Beskrywing van uitgesoekte ongunstige reaksies

ECOXAR mag renale disfunksie by die fetus veroorsaak wat tot oligohidramnios (amnionvloeistoftekort) en, in sommige gevalle, neonatale renale belemmering lei. Hierdie ongunstige effek word gemiddeld gerapporteer na dae tot weke van behandeling, alhoewel oligohidramnios minder dikwels so gou as 48 uur nadat begin is met NSAIM-terapie gerapporteer is. Oligohidramnios is dikwels, maar nie altyd nie, omkeerbaar wanneer behandeling gestaak word (sien afdelings 4.3 en 4.4).

Rapportering van vermoedelike ongunstige reaksies

Dit is belangrik om vermoedelike newe-effekte wat waargeneem word nadat die medisyne goedgekeur is te rapporteer. Dit help met volgehoue monitering van die voordeel/risiko-balans van die medisyne. Gesondheidsorgverskaffers moet asseblief enige vermoedelike newe-effekte aan SAHPRA rapporteer via die vorm om ongunstige geneesmiddelreaksies te rapporteer, wat aanlyn by SAHPRA se publikasies gevind kan word: https://www.sahpra.org.za/Publications/Index/8

4.9 Oordosering

Die mees algemeen waargenome ongewenste effekte was gastroïntestinale voorvalle en renovaskulêre voorvalle.

In die geval van oordosering, is dit raadsaam om die gewone ondersteunende maatreëls toe te pas, bv. verwyder ongeabsorbeerde materiaal vanuit die gastroïntestinale kanaal, monitor pasiënt klinies, en stel ondersteunende terapie in, indien nodig.

Etorikoksib kan nie met hemodialise gedialiseer word nie; dit is nie bekend of etorikoksib deur peritoneale dialise gedialiseer word nie.

5 FARMAKOLOGIESE EIENSKAPPE

5.1 Farmakodinamiese eienskappe

A.3.1 Antirumatika (Antiinflammatoriese Middels). ATC-kode: M01 AH05

Etorikoksib is ’n niesteroïdale antiinflammatoriese geneesmiddel (NSAIM) wat antiinflammatoriese, analgetiese en antipiretiese aktiwiteite in dieremodelle vertoon. Etorikoksib is ’n oraal aktiewe, selektiewe siklo-oksigenase-2-inhibeerder (COX-2-inhibeerder).

5.2 Farmakokinetiese eienskappe

Absorpsie

Oraal toegediende etorikoksib word geabsorbeer met ’n gemiddelde orale biobeskikbaarheid van ongeveer 100 %. Na dosering van 120 mg een keer per dag tot by ewewigsvlak, is die piek plasmakonsentrasie (geometriese gemiddelde C_{maks}=3,6 µg/mL) waargeneem teen ongeveer 1 uur (T_{maks}) na toediening aan vastende volwassenes. Die geometriese gemiddelde AOK_{0-24h} was 37,8 µg/h/mL. Die farmakokinetika van etorikoksib is lineêr regoor die kliniese dosisreikwydte.

’n Standaard maaltyd het geen klinies betekenisvolle effek op die mate of tempo van absorpsie van ’n dosis van 120 mg etorikoksib gehad nie. In gerapporteerde kliniese proewe is etorikoksib sonder inagneming van voedsel toegedien.

Die farmakokinetika van etorikoksib in 12 gesonde vrywilligers (40- tot 65-jarige ouderdom) was soortgelyk (vergelykbare AOK, C_{maks} binne ongeveer 20 %) toe dit alleen of saam met ’n magnesium/aluminiumhidroksied-teensuurmiddel of ’n kalsiumkarbonaat-teensuurmiddel toegedien is (ongeveer 50 mEkw suurneutraliserende kapasiteit).

Verspreiding

Etorikoksib is ongeveer 92 % gebonde aan plasmaproteïene oor die reeks van konsentrasies van 0,05 µg/mL tot 5 µg/mL by mense. Die volume van verspreiding by ewewigstoestand (V_{dss}) is ongeveer 120 liter. Etorikoksib kruis die plasenta en die bloedbreinskans.

Metabolisme

Etorikoksib word breedvoerig deur die lewer gemetaboliseer met < 1 % van ’n dosis wat as die moederverbinding in die urine verhaal word. Die hoofroete van metabolisme om die 6'-hidroksimetielderivaat te vorm, word gekataliseer deur sitochroom P450 (CYP) ensieme.

Vyf metaboliete is by die mens geïdentifiseer. Die hoofmetaboliet is die 6'-karboksielsuurderivaat van etorikoksib wat deur verdere oksidasie van die 6'-hidroksimetielderivaat gevorm word.

Hierdie hoofmetaboliete toon óf geen meetbare aktiwiteit nie óf slegs swak aktiwiteit as COX-2-inhibeerders.

Eliminasie

Na toediening van ’n enkele 25 mg radioaktiefgemerkte intraveneuse dosis van etorikoksib aan gesonde proefpersone, is 70 % van die radioaktiwiteit in die urine en 20 % in die feses herwin, meestal as metaboliete. Plasma en urine is versamel vir 7 dae en stoelgang is versamel vir 10 dae ná ’n dosis. Minder as 2 % is as onveranderde middel herwin.

Eliminasie van etorikoksib vind feitlik uitsluitlik deur metabolisme plaas, gevolg deur renale uitskeiding. Ewewigsvlakkonsentrasies van etorikoksib word binne 7 dae bereik, na toediening van 120 mg een keer per dag, met ’n akkumulasieverhouding van ongeveer 2, wat met ’n akkumulasiehalfleeftyd van ongeveer 22 uur ooreenstem. Die plasmaopruiming word beraam om ongeveer 50 mL/min te wees.

Bejaardes

Farmakokinetika in bejaardes (65-jarige ouderdom en ouer) met normale nierfunksie is soortgelyk aan dié in jonger persone. In gerapporteerde kliniese studies, is ’n hoër voorkoms van ongewenste ervarings waargeneem by ouer pasiënte in vergelyking met jonger pasiënte (sien afdeling 4.2).

Hepatiese belemmering

Pasiënte met geringe lewerinkorting (Child-Pughtelling 5 tot 6) wat 60 mg etorikoksib een keer per dag (vir 21 dae) ontvang het, het ongeveer ’n 16 % hoër gemiddelde AOK gehad in vergelyking met gesonde proefpersone wat dieselfde regimen ontvang het. Pasiënte met matige lewerinkorting (Child-Pughtelling 7 tot 9) wat 60 mg etorikoksib elke tweede dag (vir 21 dae) ontvang het, het soortgelyke gemiddelde AOK gehad as dié van gesonde proefpersone wat 60 mg etorikoksib een keer per dag ontvang het. Daar is geen beskikbare kliniese of farmakokinetiese data van pasiënte met ernstige lewerinkorting (Child-Pughtelling > 9) nie (sien afdelings 4.2 & 4.3).

Renale belemmering

Die farmakokinetika van ’n enkele dosis van 120 mg etorikoksib by pasiënte met matige (kreatinienopruiming 30 tot 50 mL/min) tot erge (kreatinienopruiming van < 30 mL/min) nierinkorting, en pasiënte met eindstadiumniersiekte op hemodialise, was nie beduidend verskillend van die van gesonde proefpersone nie. Hemodialise het weglaatbaar bygedra tot uitskeiding (dialise-opruiming ongeveer 50 mL/min).

Pediatriese populasie

Die farmakokinetika van etorikoksib in pediatriese pasiënte (< 12-jarige ouderdom) is nie bestudeer nie.

In ’n farmakokinetiese studie (N=16) uitgevoer in adolessente (12 tot 17 jaar oud) was die farmakokinetika in adolessente wat 40 kg tot 60 kg weeg en 60 mg etorikoksib een keer per dag ontvang het en in adolessente > 60 kg wat 90 mg etorikoksib een keer per dag ontvang het, soortgelyk aan die farmakokinetika in volwassenes wat 90 mg etorikoksib een keer per dag ontvang het. Veiligheid en doeltreffendheid van etorikoksib in pediatriese en adolessente pasiënte is nie vasgestel nie (sien afdeling 4.3).

6 FARMASEUTIESE BESONDERHEDE

6.1 Lys van hulpstowwe

- mikrokristallyne sellulose
- anhidriese kalsiumwaterstoffosfaat
- natriumkroskarmellose
- magnesiumstearaat

Deklaag:

30 mg: Opadry II groen 32K510020 (laktosemonohidraat, hipromellose, titaandioksied, triasetien, indigo-karmyn aluminiumlak, geel ysteroksied)

60 mg: Opadry II groen 35K510000 (laktosemonohidraat, hipromellose, titaandioksied, triasetien, indigo-karmyn aluminiumlak, geel ysteroksied)

90 mg: Opadry II wit 35K580003 (laktosemonohidraat, hipromellose, titaandioksied, triasetien)

120 mg: Opadry II groen 32K510018 (laktosemonohidraat, hipromellose, titaandioksied, triasetien, indigo-karmyn aluminiumlak, geel ysteroksied).

6.2 Onverenigbaarhede

Nie van toepassing nie.

6.3 Rakleeftyd

36 maande

Bewaar by of onder 25 °C.

6.4 Spesiale voorsorgmaatreëls vir berging

Beskerm teen vog. Hou die stulpstrook in die karton tot nodig vir gebruik.

6.5 Aard en inhoud van die houer

Die tablette word in koudgevormde stulpstroke verpak. Elke stulpstrook bevat 7 tablette. Die karton bevat 7 of 28 tablette.

Koudgevormde stulpstroke

'n Koudgevormde stulpstrook bestaan uit koudgevormde stulpstrooklaminaat saamgestel uit georiënteerde poliamied, aluminiumfoelie en PVC-film met 'n agterkant van harde, getemperde aluminiumfoelie, bedek met hitteseëllak aan die binnekant.

7 HOUER VAN DIE REGISTRASIESERTIFIKAAT

Ranbaxy Pharmaceuticals (Edms.) Bpk.

Lautreweg 14, Stormill, Uitbr.1

Roodepoort 1724

Suid-Afrika

8 REGISTRASIENOMMERS

ECOXAR 30 mg: 51/3.1/1144

ECOXAR 60 mg: 51/3.1/1145

ECOXAR 90 mg: 51/3.1/1146

ECOXAR 120 mg: 51/3.1/1147

9 DATUM VAN EERSTE MAGTIGING/HERNUWING VAN DIE MAGTIGING

Datum van registrasie: 11 Februarie 2020

Bemark deur Unicorn Pharmaceuticals (Edms.) Bpk.

10 DATUM VAN HERSIENING VAN DIE TEKS

21 January 2022

* ECOXAR 30 mg word nie bemark nie. Vir hierdie dosis kan 30 mg etorikoksib van 'n ander handelsmerk gebruik word.