PROFESSIONAL INFORMATION FOR EXXIB

SCHEDULING STATUS

S3

1. NAME OF THE MEDICINE

EXXIB 60 film coated tablets

EXXIB 90 film coated tablets

EXXIB 120 film coated tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

EXXIB 60: Each film coated tablet contains 60 mg etoricoxib.

EXXIB 90: Each film coated tablet contains 90 mg etoricoxib.

EXXIB 120: Each film coated tablet contains 120 mg etoricoxib.

EXXIB 60: Contains sugar (1,68 mg lactose monohydrate per tablet).

EXXIB 90: Contains sugar (2,52 mg lactose monohydrate per tablet).

EXXIB 120: Contains sugar (3,36 mg lactose monohydrate per tablet).

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film coated tablet

EXXIB 60: Green, round, biconvex, film coated tablets debossed with '444' on one side and 'L' on the other side.

EXXIB 90: White to off-white, round, biconvex, film coated tablets debossed with '445' on one side and 'L' on the other side.

EXXIB 120: Pale-green, round, biconvex, film coated tablets debossed with '446' on one side and 'L' on the other side.

4. CLINICAL PARTICULARS

PROFESSIONAL INFORMATION FOR EXXIB

4.1 Therapeutic indications

EXXIB is indicated for the:

- symptomatic relief of 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:

EXXIB is administered orally and may be taken with or without food.

Use the lowest effective dose for the shortest possible duration of treatment.

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.

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, which should only be used for the acute symptomatic period, 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 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 post-operative acute dental surgery pain should not exceed 90 mg daily.

As the cardiovascular risks of EXXIB 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).

Elderly:

No dosage adjustment in EXXIB is necessary for the elderly. Although the elderly may be more susceptible to renal, gastrointestinal and cardiovascular side effects (see sections 4.4 and 4.8).

When using EXXIB 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.

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.

EXXIB should not be given to patients with severe hepatic impairment (Child-Pugh score > 9) (see section 4.3).

Renal insufficiency:

No dosage adjustment is necessary for patients with a creatinine clearance ≥ 30 mL/min. The use of EXXIB in patients with creatinine clearance < 30 mL/min is contraindicated (see section 4.3).

Method of administration:

Oral.

4.3 Contraindications

- Known hypersensitivity to etoricoxib or to any of the inactive ingredients of EXXIB.
- Patients with active peptic ulceration or gastrointestinal (GI) bleeding.
- Patients with severe hepatic dysfunction (Child-Pugh score > 9 or serum albumin < 25 g/L).
- 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 nonsteroidal anti-inflammatory drugs (NSAIDs), including COX-2 inhibitors.
- Hypertension which has not been adequately controlled.
- Pregnancy and lactation (see section 4.6).
- Children and adolescents under the age of 16 years.
- Patients with inflammatory bowel disease.
- Patients with moderate to severe heart failure (NYHA class II – IV).
- Established ischaemic heart disease, peripheral arterial disease and/or cerebrovascular disease.
- Perioperative analgesia in the setting of coronary artery bypass surgery.
- Lithium therapy: Concomitant administration with EXXIB may lead to toxic blood concentrations of lithium (see section 4.5).
- Digoxin: Co-administration with EXXIB may lead to toxic blood concentrations of digoxin (see section 4.5).

4.4 Special warnings and precautions for use

EXXIB may predispose to cardiovascular events, gastrointestinal (GI) events or cutaneous reactions, which may be fatal.

Gastrointestinal effects:

Upper gastrointestinal complications [perforations, ulcers or bleedings (PUBs)], some of them resulting in fatal outcome, have occurred in patients treated with EXXIB.

Caution is advised with treatment of patients most at risk of developing a gastrointestinal complication with NSAIDs such as EXXIB: the elderly, patients using any other NSAID or aspirin 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 side effects (gastrointestinal ulceration or other gastrointestinal complications) when EXXIB is taken concomitantly with aspirin (even at low doses).

Cardiovascular effects:

EXXIB may be associated with a risk of thrombotic events (especially myocardial infarction and stroke). As the cardiovascular risks of EXXIB 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 or smoking) should only be treated with EXXIB after careful consideration.

EXXIB is not a substitute for aspirin for prophylaxis of cardiovascular thromboembolic diseases, because of its lack of antiplatelet effect on platelets. Antiplatelet therapies should therefore not be discontinued (see section 4.5). There is no evidence that concurrent use of aspirin mitigates the increased risk of serious cardiovascular thrombotic events associated with EXXIB.

Renal effects:

Renal prostaglandins may play a compensatory role in the maintenance of renal perfusion. Therefore, under conditions of compromised renal perfusion, administration of EXXIB 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.

Severe hypokalaemia and renal tubular acidosis (RTA) have been reported with the prolonged use of other NSAIDs (such as ibuprofen) at higher than recommended doses. Caution is advised with the use of EXXIB.

Fluid retention, oedema and hypertension:

Caution should be exercised when initiating treatment with EXXIB in patients with dehydration. It is advisable to rehydrate patients prior to starting therapy with EXXIB. Due to inhibition of prostaglandin synthesis, fluid retention, oedema and hypertension have been observed in patients taking EXXIB. EXXIB 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.

EXXIB can be associated with new onset or recurrent congestive heart failure (see section 4.8). 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 EXXIB should be considered.

EXXIB may be associated with more frequent and severe hypertension than some other NSAIDs and selective COX-2 inhibitors, particularly at high doses. Special attention should be paid to blood pressure monitoring during the treatment with EXXIB. If blood pressure rises significantly, alternative treatment should be considered.

Hepatic effects:

Any patients with symptoms and/or signs suggesting liver dysfunction, or in whom an

abnormal liver function test has occurred, should be monitored. EXXIB should be discontinued if signs of hepatic insufficiency occur, or if persistently abnormal liver function tests (three times the upper limit of normal) are detected. Elevations of alanine aminotransferase (ALT) and/or aspartate aminotransferase (AST) (approximately 3 times the upper limit of normal) have been reported in approximately 1 % of patients in clinical trials treated for up to one year with etoricoxib 60 mg or 90 mg.

Skin reactions:

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 EXXIB (see section 4.8). Patients appear to be at highest risk for these reactions early in the course of therapy, with 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 EXXIB (see section 4.8). Selective COX-2 inhibitors have been associated with an increased risk of skin reactions in patients with a history of an allergy. EXXIB should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity.

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

When using EXXIB 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.

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

Excipient warnings:

EXXIB contains lactose monohydrate.

Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose/galactose malabsorption should not take EXXIB.

4.5 Interaction with other medicines and other forms of interaction

Warfarin:

Patients receiving warfarin should be closely monitored for their prothrombin time or international normalised ratio (INR), particularly in the first few days when therapy with EXXIB is initiated or the dose of EXXIB is changed.

Diuretics, ACE inhibitors and angiotensin II antagonists:

EXXIB may diminish the antihypertensive effect of diuretics, ACE inhibitors and angiotensin receptor blockers. This interaction should be given consideration in patients taking EXXIB concomitantly with these medicines.

In some patients with compromised renal function, (e.g. dehydrated patients or elderly patients with compromised renal function) the co-administration of an ACE inhibitor or angiotensin receptor blockers may result in further deterioration of renal function, including possible acute renal failure, which may be reversible.
These interactions should be considered in patients taking EXXIB concomitantly with ACE inhibitors or angiotensin receptor blockers. Therefore the combination should be administered with caution, especially in the elderly and patients with impaired renal function. Patients should be adequately hydrated and monitoring of renal function at initiation and periodically thereafter could be considered with concomitant therapy.

Aspirin:

EXXIB can be used concomitantly with aspirin at doses used for cardiovascular prophylaxis (low-dose aspirin). However, concomitant administration of low-dose aspirin with EXXIB may result in an increased rate of GI ulceration or other complications compared to use of EXXIB alone. Concomitant administration of EXXIB with doses of aspirin above those for cardiovascular prophylaxis or with other NSAIDs is not recommended (see section 4.4).

Because of its lack of platelet effects, EXXIB is not a substitute for aspirin for cardiovascular prophylaxis.

There is no evidence that concurrent use of aspirin mitigates the increased risk of serious cardiovascular thrombotic events associated with EXXIB.

Ciclosporin and tacrolimus:

Although this interaction has not been studied with EXXIB, co-administration of ciclosporin or tacrolimus with any NSAID such as EXXIB may increase the nephrotoxic effect of ciclosporin or tacrolimus. Renal function should be monitored when EXXIB and either of these medicines are used in combination.

Lithium:

NSAIDs and selective COX-2 inhibitors such as EXXIB may increase plasma lithium levels. This interaction should be considered in patients taking EXXIB concomitantly with lithium.

Methotrexate:

EXXIB 120 mg increased methotrexate plasma concentrations by 28 % and reduced renal clearance of methotrexate by 13 %. Adequate monitoring for methotrexate-related toxicity is recommended when EXXIB at dosages > 90 mg daily and methotrexate are administered concomitantly.

Oral contraceptives:

EXXIB is an inhibitor of human sulphotransferase activity and has been shown to increase the plasma concentration of ethinyl oestradiol (EO).

This increase in EO concentration should be considered when selecting an oral contraceptive for use with EXXIB. An increase in EO exposure can increase the incidence of side effects associated with oral contraceptives (e.g. venous thromboembolic events in women at risk).

Hormone replacement therapy (HRT):

The effects of EXXIB 120 on the exposure ($AUC_{0\text{-}24hr}$) to conjugated oestrogens were less than half of those observed when conjugated oestrogen 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 conjugated oestrogens were not studied in combination with EXXIB. These increases in oestrogenic concentration should be taken into consideration when selecting post-menopausal hormone therapy for use with EXXIB because the increase in oestrogen exposure may increase the risk of side effects associated with HRT.

Prednisone or prednisolone:

EXXIB did not have clinically important effects on the pharmacokinetics of prednisone or prednisolone.

Digoxin:

EXXIB 120 did not alter the steady-state plasma AUC0-24hr or renal elimination of digoxin. There was an increase in digoxin C_{max} in healthy volunteers (approximately 33 %) (see section 4.3).

Effect of EXXIB on medicines metabolised by sulphotransferases:

EXXIB is an inhibitor of human sulphotransferase activity, and has been shown to increase the serum concentrations of ethinyl oestradiol. Care should be exercised when administering EXXIB concurrently with other medicines primarily

metabolised by human sulphotransferases (e.g. oral salbutamol and minoxidil).

Ketoconazole:

Ketoconazole, a potent inhibitor of CYP3A4, did not have any clinically important effect on the single-dose pharmacokinetics of 60 mg EXXIB (43 % increase in AUC).

Rifampicin:

Co-administration of EXXIB with rifampicin, a potent inducer of CYP enzymes, produced a 65 % decrease in EXXIB plasma concentrations. This interaction should be considered when EXXIB is co-administered with rifampicin.

Antacids:

Antacids do not affect the pharmacokinetics of EXXIB to a clinically relevant extent.

Furosemide:

EXXIB may reduce the natriuretic effect of furosemide and hydrochlorothiazide.

4.6 Fertility, pregnancy and lactation

EXXIB is contraindicated in pregnancy and lactation (see section 4.3).

Pregnancy

EXXIB is contraindicated in pregnancy (see section 4.3)

Regular use of NSAIDs may result in:

First trimester:

Inhibition of prostaglandin synthesis may adversely affect the pregnancy and/or the embryo/foetal development. Data from epidemiological studies raise concern about an increased risk of miscarriage and of cardiac malformation and gastroschisis after use of a prostaglandin synthesis inhibitor in early pregnancy. The absolute

risk for cardiovascular malformation was increased from less than 1 %, up to approximately 1,5 %. In animals, administration of a prostaglandin synthesis inhibitor has been shown to result in increased pre- and post-implantation loss and embryo-foetal lethality. In addition, increased incidences of various malformations including cardiovascular, have been reported in animals given a prostaglandin synthesis inhibitor during the organogenetic period.

Second and Third trimester

During the third trimester of pregnancy, prostaglandin synthesis inhibitors, may expose the foetus to: cardiopulmonary toxicity (with premature closure of the ductus arteriosus and pulmonary hypertension); renal dysfunction, which may progress to renal failure with oligo-hydroamniosis.

At the end of pregnancy, the mother and the neonate may be exposed to: possible prolongation of bleeding time, an anti-aggregating effect which may occur even at very low doses; inhibition of uterine contractions resulting in delayed or prolonged labour.

Breastfeeding

Limited data indicate that EXXIB is excreted in breast milk and must therefore not be used during lactation.

Fertility

Based on the mechanism of action, the use of NSAIDs, including EXXIB, may delay or prevent rupture of ovarian follicles, which has been associated with reversible infertility in some women.

4.7 Effects on ability to drive and use machines

Patients who experience dizziness, vertigo or somnolence while taking EXXIB should

refrain from driving or operating machinery.

4.8 Undesirable effects

Tabulated list of adverse reactions:

System Organ Class	**Frequency**	**Side effects**
Infections and infestations	Frequent Less frequent	Alveolar osteitis. Gastroenteritis, upper respiratory infection, urinary tract infection.
Blood and the lymphatic system disorders	Less frequent Frequency unknown	Anaemia (primarily associated with gastrointestinal bleeding), leucopenia. Thrombocytopenia.
Immune system disorders	Frequent 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, decreased mental acuity. Confusion, hallucinations, restlessness.
Nervous system disorders	Frequent Less frequent	Dizziness, headache. Insomnia,

		paraesthesia/hypaesthesia, cerebrovascular incidents (stroke).
	Frequency unknown	Somnolence, dysgeusia
Eye disorders	Less frequent	Conjunctivitis.
	Frequency unknown	Blurred vision.
Ear and labyrinth disorders	Less frequent	Tinnitus, vertigo.
Cardiac disorders	Frequent	Palpitations.
	Less frequent	Atrial fibrillation, congestive heart failure, non-specific ECG changes, myocardial infarction, angina.
	Frequency unknown	Dysrhythmia, tachycardia, cardiovascular thrombotic events.
Vascular disorders	Frequent	Hypertension.
	Less frequent	Flushing, transient ischaemic attack, hypertensive crisis.
	Frequency unknown	Aggravated hypertension, peripheral oedema.
Respiratory, thoracic and mediastinal disorders	Less frequent	Coughing, dyspnoea, epistaxis.
	Frequency unknown	Bronchospasm.
Gastrointestinal disorders	Frequent	Abdominal pain, flatulence, heartburn, diarrhoea,

		dyspepsia, epigastric discomfort, nausea.
	Less frequent	Abdominal distention, acid reflux, bowel movement pattern change, constipation, dry mouth, gastroduodenal ulcer, irritable bowel syndrome, oesophagitis, oral ulcer, vomiting, gastritis, pancreatitis.
	Frequency unknown	Peptic ulcers including gastrointestinal perforation and Bleeding (mainly in the elderly).
Hepato-biliary disorders	Frequent	Increased ALT, increased AST.
	Frequency unknown	Hepatitis, jaundice, hepatic failure
Skin and subcutaneous tissue disorders	Frequent	Ecchymosis.
	Less frequent	Facial oedema, pruritus, rash, erythema.
	Frequency unknown:	Urticaria, Stevens-Johnson syndrome, toxic epidermal necrolysis, fixed drug eruption.
Musculoskeletal, and connective tissue disorders	Less frequent	Muscular cramp/spasm, musculoskeletal pain/stiffness.

Renal and urinary disorders	Less frequent Frequency unknown	Proteinuria. Renal insufficiency, including renal failure nephrotoxicity including interstitial nephritis and nephrotic syndrome.
General disorders and administration site conditions	Frequent Less frequent	Asthenia, fatigue, flu-like symptoms. Chest pain.
Investigations	Less frequent	Increased blood urea, increased creatine phosphokinase, decreased haematocrit, decreased haemoglobin, hyperkalaemia, decreased leukocytes, decreased platelets, increased serum creatinine, increased uric acid, decreased blood sodium.

The following serious side effects have been reported in association with the use of NSAIDs and cannot be ruled out for EXXIB: nephrotoxicity including interstitial nephritis and nephrotic syndrome; renal tubular acidosis; hepatotoxicity including hepatic failure, jaundice and pancreatitis; hypokalaemia.

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 providers are requested to report any suspected adverse drug reactions to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website.

4.9 Overdose

The most frequently observed side effects were consistent with the safety profile of EXXIB (e.g. GI events, renovascular events). In the event of overdose, appropriate supportive medical care should be provided (remove unabsorbed material from the gastrointestinal tract, employ clinical monitoring, and institute supportive therapy if required).

EXXIB is not dialysable by haemodialysis. It is not known whether EXXIB is dialysable by peritoneal dialysis.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic Properties

A 3.1 Antirheumatics (anti-inflammatory agents)

Pharmacotherapeutic group: Anti-inflammatory and antirheumatic products, non-steroids, coxibs.

ATC code: M01AH01.

Etoricoxib is a nonsteroidal anti-inflammatory drug (NSAID) that exhibits anti-inflammatory, analgesic and antipyretic activities in animal models.

Etoricoxib is an orally active, selective cyclooxygenase-2 (COX-2) inhibitor.

5.2 Pharmacokinetic Properties

Absorption

Etoricoxib is well absorbed from the gastrointestinal tract after oral doses. The absolute bioavailability is approximately 100 %. Following a 120 mg once daily

dosing to steady state, the peak plasma concentration (geometric mean C_{max} equal to 3,6 µg/mL) was observed at approximately 1 hour (T_{max}) after administration to fasted adults. The geometric mean area under the curve (AUC_{0-24hr}) was 37,8 µg/h/mL. The pharmacokinetics of etoricoxib are linear across the clinical dose range.
Dosing with food (a standard meal) had no meaningful effect on the extent or rate of absorption of etoricoxib after administration of a 120 mg dose.

Distribution

Etoricoxib is approximately 92 % bound to plasma protein over the range of concentrations of 0,05 to 5 µg/mL in humans. The volume of distribution at steady state (Vdss) was approximately120 L in humans. Etoricoxib crosses the placenta and the blood-brain barrier.

Biotransformation

Etoricoxib is extensively metabolised with less than 1 % of a dose recovered in urine as the parent drug. The major route of metabolism is via cytochrome P450 isoenzymes including CYP3A4 to form the 6'-hydroxymethyl derivative of etoricoxib, which is then oxidised to the 6'-carboxylic acid derivative, the major metabolite. Both are inactive or only weak cyclooxygenase-2 (COX-2) inhibitors.

Elimination

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

Special populations

Elderly:

Pharmacokinetics in the elderly with normal renal function (65 years of age and older) are similar to those in the young. A higher incidence of adverse effects was seen in older patients.

Hepatic insufficiency:

Patients with mild hepatic dysfunction (Child-Pugh score 5 to 6) who were 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 dysfunction (Child-Pugh score 7 to 9) who were administered etoricoxib 60 mg every other day, had similar mean AUC compared to the healthy subjects given etoricoxib 60 mg once daily. There are no clinical or pharmacokinetic data in patients with severe hepatic dysfunction (Child-Pugh score > 9) (see sections 4.2 and 4.3).

Renal insufficiency:

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

Paediatric patients:

The pharmacokinetics of etoricoxib in paediatric patients (less than 12 years old) has not been studied.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Anhydrous calcium phosphate dibasic

Croscarmellose sodium

Hydroxypropyl cellulose

Magnesium stearate

Microcrystalline cellulose

Opadry Green (EXXIB 60 and EXXIB 120)

FD&C Blue # 2/indigo carmine aluminium lake

Hypromellose

Iron oxide yellow,

Lactose monohydrate,

Titanium dioxide

Triacetin

Opadry White (EXXIB 90)

Hypromellose

Lactose monohydrate

Titanium dioxide

Triacetin

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 Months

6.4 Special precautions for storage

Store at or below 30 °C.

Protect from moisture.

Do not remove blister strips from outer carton until required for use.

6.5 Nature and contents of container

Silver aluminium/CFB foil blister strips, or silver aluminium foil and transparent PVC/PVDC or PVC/PE/PVDC film blister strips. Each blister strip contains 8 or 10 tablets

Pack size: 8 or 30 tablets packed into a cardboard box.

6.6 Special precautions for disposal and other handling

Any unused medicine or waste material should be disposed of in accordance with local requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Activo Health (Pty) Ltd
Block B, Arena Office Park
272 West Avenue
Centurion
0157
South Africa

8. REGISTRATION NUMBERS

EXXIB 60: 50/3.1/0087

EXXIB 90: 50/3.1/0088

EXXIB 120: 50/3.1/0089

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of registration: 28 November 2019

10. DATE OF REVISION OF THE TEXT

27 February 2025