PROFESSIONAL INFORMATION FOR

ETIFLAM 60

ETIFLAM 90

ETIFLAM 120

SCHEDULING STATUS

S3

1. NAME OF THE MEDICINE

ETIFLAM 60 (60 mg, film-coated tablets)

ETIFLAM 90 (90 mg, film-coated tablets)

ETIFLAM 120 (120 mg, film-coated tablets)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

ETIFLAM 60: Each film-coated tablet contains etoricoxib 60 mg.

Contains sugar: Lactose monohydrate (2,8 mg).

ETIFLAM 90: Each film-coated tablet contains etoricoxib 90 mg

Contains sugar: Lactose monohydrate (4,2 mg).

ETIFLAM 120: Each film-coated tablet contains etoricoxib 120 mg.

Contains sugar: Lactose monohydrate (5,6 mg).

For the full list of excipients, see **section 6.1**.

3. PHARMACEUTICAL FORM

ETIFLAM 60: White to off-white, apple shaped, biconvex film-coated tablet debossed with “C2” on one side and plain on the other side.

ETIFLAM 90: Dark green, apple shaped, biconvex film-coated tablet debossed with “C3” on one side and plain on the other side.

ETIFLAM 120: Dark green, apple shaped, biconvex film-coated tablet debossed with “C4” on one side and plain on the other side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

ETIFLAM film-coated tablets are indicated for:

- 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

Rheumatoid arthritis (RA)

The recommended dose is 90 mg once per day. In some patients, 60 mg once daily may provide adequate therapeutic benefit.

Ankylosing spondylitis (AS)

The recommended dose is 90 mg once per day. In some patients, 60 mg once daily may provide adequate therapeutic benefit.

Short-term relief of acute pain

The recommended dose is 90 or 120 mg once per day. The treatment period must not exceed 8 days.

Acute gouty arthritis

The recommended dose is 120 mg once per day. The treatment period must not exceed 8 days.

Primary dysmenorrhoea

The recommended dose is 120 mg once per day.

Post-operative dental pain

The recommended dose is 90 mg once per day.

There are no data to support doses higher than those recommended for the indication.

Therefore:

The dose for Rheumatoid Arthritis (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.

DO NOT EXCEED THE RECOMMENDED DOSES.

The risk of cardiovascular adverse events is increased with the higher doses and prolonged treatment periods. Therefore, the lowest effective dose should be used for the shortest treatment duration possible. The patient's need for symptomatic relief and response to therapy should be re-evaluated periodically (see **section 4.4**).

Special populations

Elderly

No dose adjustments are required for patients older than 65 years of age. Although the elderly may be more susceptible to renal, gastrointestinal and cardiovascular adverse events (see **section 4.4** and **4.8**). When using ETIFLAM 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 ETIFLAM

Hepatic dysfunction

A once daily dose of 60 mg should not be exceeded in patients with mild hepatic impairment (Child-Pugh score 5 to 6).

Doses should be reduced in patients with moderate hepatic impairment (Child-Pugh score 7 - 9). The recommended dose of 60 mg every other day should not be exceeded.

There are no data to support use in patients with severe hepatic impairment (Child-Pugh higher than 9). ETIFLAM is contraindicated in these patients (see **section 4.3** and **5.0**).

Renal impairment

No dose adjustments are required in patients with mild to moderate renal impairment (creatinine clearance ≥ 30 mL/min). ETIFLAM is contraindicated in patients with creatinine clearance less than 30 mL/min (see **section 4.3**).

Paediatric population

The safety and efficacy of ETIFLAM in children has not yet been established

Method of administration

ETIFLAM is administered orally. It may be taken with or without food. Use the lowest effective dose for the shortest possible duration of treatment.

4.3 Contraindications

ETIFLAM film-coated tablets are contraindicated in:

- Patients with known hypersensitivity to etoricoxib or any of the other ingredients of ETIFLAM
- Patients with active peptic ulceration or gastrointestinal (GI) bleeding
- Patients with severe hepatic insufficiency (Child-Pugh score greater than 9 or serum albumin less than 25 g/L)
- Patients with estimated creatinine clearance of less than 30 mL/min
- Patients who have developed signs of asthma, acute rhinitis, nasal polyps, angioedema or urticaria following administration of aspirin or other non-steroidal anti-inflammatory drugs (NSAIDS) including ETIFLAM
- Uncontrolled hypertension
- Pregnancy and lactation (see **section 4.6**)
- 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 and/or cerebrovascular disease (stroke) and peripheral arterial disease (see **section 4.4**)
- Peri-operative analgesia in the setting of coronary artery bypass surgery (CABG)
- Patients who are receiving concomitant lithium therapy with ETIFLAM as this increases plasma levels of lithium (see **section 4.5**)
- Patients who are at high risk of digoxin toxicity as concomitant use of ETIFLAM with digoxin may increase C_{max} of digoxin by approximately 33 %.

4.4 Special warnings and precautions for use

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

Risk of renal tubular acidosis and hypokalaemia are associated with non-steroidal anti-inflammatory medicine (NSAID) usage.

Hypersensitivity reactions

Serious skin reactions (such as exfoliative dermatitis, Steven-Johnson syndrome and toxic epidermal necrolysis) which may be fatal can occur. Serious hypersensitivity reactions like anaphylaxis and angioedema have been reported (see **section 4.8**).

There is a high risk of skin reactions in patients with a history of allergies. Treatment should be discontinued at the first appearance of skin rash, mucosal lesions or any other sign of allergy.

Cardiovascular effects

Caution is advised when ETIFLAM is prescribed to patients with cardiovascular risk factors such as hypertension, diabetes, smoking and hypercholesterolaemia.

Due to inhibition of prostaglandin synthesis, fluid retention and oedema have been observed in patients taking ETIFLAM, therefore ETIFLAM 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 NSAIDs like ETIFLAM can be associated with new onset or recurrent congestive heart failure. Therefore, ETIFLAM must be used with caution in patients with a history of heart diseases, left ventricular dysfunction or hypertension or in patients with pre-existing oedema from any other

reason. Should the conditions of these patients exacerbate further, appropriate measures including discontinuation of treatment should be taken.

ETIFLAM may cause more frequent and severe hypertension than other NSAIDS and COX-2 inhibitors. Therefore, blood pressure monitoring is advised during treatment with ETIFLAM. If blood pressure increases significantly, alternative treatments should be considered.

The selective COX-2 inhibitor class of medicines, to which ETIFLAM belongs, is associated with a high risk of thrombotic events, especially myocardial infarction and stroke. Prolonged treatment periods and high doses increase the risk of cardiovascular events. Therefore, the lowest effective doses and shortest treatment periods possible should be used during treatment with ETIFLAM. The patient's need for symptomatic relief and response to therapy must be assessed periodically.

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

Gastrointestinal effects

ETIFLAM can cause upper gastrointestinal complications such as perforations, ulcers or bleeding (PUBs), some of which may be fatal. Caution should be exercised during administration in patients with high risk factors such as patients using any other NSAIDs (including aspirin) concurrently, or those with pre-existing gastrointestinal complications [perforations, ulcers or bleeding (PUBS) and the elderly]. Concurrent use with aspirin, even at low doses, carries a high risk of gastrointestinal events like ulceration and bleeding.

There appears to be a higher risk for cardiovascular events with higher doses and longer duration of treatment.

Caution is advised when treatment is initiated in patients with dehydration. Rehydration should occur prior to initiating ETIFLAM treatment in dehydrated patients.

Because of its lack of platelet effect, ETIFLAM is not a substitute for aspirin in cardiovascular prophylaxis. Because ETIFLAM does not inhibit platelet aggregation, anti-platelet therapies should not be discontinued, but should be considered in patients with increased risk factors or with a history of cardiovascular or thrombotic events. There is no evidence to suggest that concurrent use with aspirin alleviates the increased risk of serious cardiovascular thrombotic events (see **section 4.5**).

Extreme caution is advised and appropriate medical monitoring should occur during treatment in the elderly and in patients with cardiac, hepatic or renal impairment. If conditions of these patients are aggravated during ETIFLAM therapy, appropriate measures including discontinuation of treatment, should occur.

Long-term administration of NSAIDs such as ETIFLAM may result 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 ETIFLAM may cause a reduction in prostaglandin formation and secondarily, in renal blood flow and thereby impairing renal function. Patients who have significantly impaired pre-existing renal function, uncompensated heart failure or liver cirrhosis are at great risk of developing impaired renal function. Monitoring of renal and hepatic function in such patients is required.

Elevations of alanine aminotransferase (ALT) and 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 up to one year with ETIFLAM 60 mg and 90 mg daily.

Patients with signs of liver dysfunction or abnormal liver function tests should be evaluated for abnormal liver enzyme activity regularly. Treatment should be discontinued if abnormal liver function tests (3 times the upper limit of normal) are observed.

ETIFLAM may mask fever or other symptoms of inflammation or infections.

Lactose

ETIFLAM film-coated tablets contain lactose. Patients with the rare hereditary problems of galactose intolerance total lactase deficiency or glucose-galactose malabsorption should not take ETIFLAM.

4.5 Interaction with other medicinal products and other forms of interaction

Ciclosporin and tacrolimus

Concurrent use of ETIFLAM or any other NSAID can cause nephrotoxicity due to ciclosporin or tacrolimus. Renal function should be monitored when ETIFLAM is co-administered with ciclosporin or tacrolimus.

Warfarin

ETIFLAM daily doses of 120 mg in patients that were on warfarin treatment were associated with approximately 13 % increases in prothrombin time International Normalised Ratio (INR). INR

values should be monitored periodically during co-administration with warfarin or similar medicines.

Rifampicin

Rifampicin has been reported to reduce etoricoxib exposure by 65 % due to its role in induction of hepatic metabolism. This effect should be considered prior to its simultaneous use with ETIFLAM.

Methotrexate

Doses of ETIFLAM 120 mg have been reported to increase methotrexate exposure (AUC) by 28 % and reduce renal clearance by 13 %. The risk of methotrexate toxicity should be taken into account when high doses (above 90 mg per day) of ETIFLAM is administered concomitantly with methotrexate.

Diuretics, angiotensin converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs)

Non-selective NSAIDS and COX-2 inhibitors such as ETIFLAM have been reported to reduce the antihypertensive effects of diuretics.

Concurrent use of ETIFLAM with ACE inhibitors or ARBs in patients with compromised renal function (such as the elderly or volume depleted patients including those on diuretic therapy) can exacerbate renal function further or even lead to acute renal failure, which may be reversible. Caution is advised during co-administration, especially in the elderly or in patients

with renal insufficiency. Patients should be hydrated properly prior to initiation of therapy. Renal function should be monitored at the start and during therapy.

Lithium

ETIFLAM may increase lithium plasma levels. This interaction should be taken into account during their co-administration.

Aspirin

Once daily doses (120 mg) of ETIFLAM do not have an effect on the anti-platelet activity of aspirin (81 mg per day). ETIFLAM may be used concomitantly with aspirin at dosage levels (or low doses) used for cardiovascular prophylaxis. However, simultaneous use even at this level increases the risk of gastrointestinal complications (ulcers and bleeding) when compared to when ETIFLAM is used alone. Therefore, simultaneous intake of aspirin at levels above doses used for cardiovascular prophylaxis is not recommended (see **section 4.4**).

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

Oral contraceptives

ETIFLAM must be given with care when used in women on oral contraceptive therapy, particularly those taking ethinyl oestradiol (EE). Doses of ETIFLAM (at 60 and 120 mg) given with EE 35 µg and 0,5 to 1 mg norethindrone (NET) raised the steady state of EE $AUC_{(0-24)}$ by 37 % and 50 - 60 %, respectively, with no clinically relevant effect on NET. Raised EE levels may increase the incidence of adverse events (such as venous thromboembolic events) in women.

Furosemide

ETIFLAM decreases natriuretic and antihypertensive effects of furosemide and thiazides. This effect has been attributed to inhibition of renal prostaglandin synthesis.

Hormone replacement therapy (HRT)

ETIFLAM doses of 120 mg administered together with HRT consisting of 0,625 mg conjugated oestrogens for 28 days increased mean steady state $AUC_{(0-24h)}$ of unconjugated oestrone by 41 %, equilin by 76 % and 17-beta-oestradiol by 22 %. The effects of ETIFLAM 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 are unknown, and higher doses of conjugated oestrogens were not studied in combination with ETIFLAM. These interactions must be considered when prescribing ETIFLAM to women taking HRT as the extended oestrogen exposure increases the risk of oestrogen-related adverse events.

Antivirals

Concomitant use of NSAIDs such as ETIFLAM with zidovudine increases the risk of haematotoxicity.

Ritonavir can raise NSAIDs', such as ETIFLAM 's, plasma concentrations, thereby increasing the incidence of ETIFLAM -related adverse events.

Effects on medicines metabolised by sulfotransferases

ETIFLAM inhibits human sulfotransferases, particularly SULT1E1 and it has been demonstrated to raise plasma concentrations of ethinyl oestradiol. Prescribers should exercise caution when using ETIFLAM together with other medicines metabolised by human sulfotransferases such as oral salbutamol and minoxidil.

There have been reports of a 33 % increase in digoxin C_{max} levels in healthy volunteers (see **section 4.3**).

Other

Use of more than one NSAID together should be avoided because of the risk of adverse events.

The risk of gastrointestinal bleeding and ulceration associated with NSAIDs is increased when used with corticosteroids, selective serotonin reuptake inhibitors (SSRIs), venlafaxine, anti-platelets (clopidogrel and ticlopidine), iloprost, erlotinib, sibutramine, alcohol, bisphosphonates or pentoxifylline.

4.6 Fertility, pregnancy and lactation

Women of childbearing potential / Contraception in males and females

ETIFLAM is not recommended in fertile women trying to conceive.

Pregnancy

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

No clinical data is available on exposed pregnancies for etoricoxib. Animal studies have shown reproductive toxicity. The potential for human risk in pregnancy is unknown. Etoricoxib, as with other medicinal products inhibiting prostaglandin synthesis, may cause uterine inertia and premature closure of the ductus arteriosus during the last trimester.

4.7 Effects on ability to drive and use machines

Dizziness, asthenia and blurred vision may occur. Patients who experience these side effects should exercise caution as these side effects can impair the ability to drive and operate machinery.

4.8 Undesirable effects

Infections and infestation

Frequent: Alveolar osteitis.

Less frequent: Gastroenteritis, upper respiratory tract infection, urinary tract infection.

Blood and lymphatic system disorders

Less frequent: Anaemia (primarily associated with gastrointestinal bleeding), leukopenia.

Frequency unknown: Thrombocytopenia.

Metabolism and nutrition disorders

Frequent: Oedema or fluid retention.

Less frequent: Increased or decreased appetite, weight gain.

Psychiatric disorders

Less frequent: Anxiety, mental acuity decreased.

Frequency unknown: Confusion, hallucinations, depression, restlessness.

Nervous system disorders

Frequent: Dizziness, headache.

Less frequent: Insomnia, paraesthesia / hypoesthesia, aseptic meningitis.

Frequency unknown: Dysgeusia, somnolence, cerebrovascular incidents (strokes).

Eye disorders

Less frequent: Conjunctivitis.

Frequency Unknown: Blurred vision, photosensitivity.

Ear and labyrinth disorders

Less frequent: Tinnitus, vertigo.

Cardiac disorders

Frequent: Palpitations.

Less frequent: Congestive cardiac failure, myocardial infarction, cardiovascular thrombotic events, atrial fibrillation, angina, non-specific ECG changes.

Frequency unknown: Dysrhythmia, tachycardia, aggravated hypertension.

Vascular disorders

Frequent: Hypertension.

Less frequent: Flushing, transient ischaemic attack, peripheral oedema, vasculitis.

Frequency unknown: Hypertensive crisis, aggravated hypertension.

Respiratory, thoracic and mediastinal disorders

Less frequent: Cough, dyspnoea, epistaxis.

Frequency unknown: Bronchospasm.

Gastrointestinal disorders

Frequent: Gastrointestinal complications (such as abdominal pain, flatulence and/or heartburn), diarrhoea, dyspepsia, epigastric discomfort, nausea.

Less frequent: Abdominal distension, acid reflux, bowel movement pattern change, constipation, dry mouth, gastro-duodenal ulcer, irritable bowel syndrome, oral ulcer, vomiting, gastritis pancreatitis.

Frequency unknown: Peptic ulcers including gastrointestinal perforation, and bleeding (mostly in the elderly).

Skin and subcutaneous tissue disorders

Frequent: Ecchymosis.

Less frequent: Facial oedema, pruritus, rash, erythema.

Frequency unknown: Steven-Johnson syndrome, toxic epidermal necrolysis, urticaria, fixed drug eruption.

Musculoskeletal, connective tissue and bone disorders

Less frequent: Muscular cramps or spasms, musculoskeletal pain, stiffness.

Renal and urinary system disorders

Less frequent: Proteinuria.

Frequency unknown: Renal insufficiency including renal failure (see **section 5.2**), nephrotoxicity including interstitial nephritis and nephrotic syndrome.

Hepato-biliary disorders

Frequency unknown: Hepatitis, jaundice, hepatic failure, hepatotoxicity including pancreatitis.

General disorders and administrative site conditions

Frequent: Asthenia / fatigue, flu-like disease.

Less frequent: Chest pain.

Immune system disorders

Frequency unknown: Hypersensitivity reactions including angioedema, anaphylactic/ anaphylactoid reactions including shock.

Investigations

Frequent: Raised liver enzyme activity (ALT and AST).

Less frequent: Blood urea increased, creatinine phosphokinase increased, haematocrit decreased, haemoglobin decreased, hyperkalaemia, leukocytes decreased, platelets decreased, serum creatinine increased, uric acid increased, blood sodium decreased.

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 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 or to Cipla Medpro (Pty) Ltd at drugsafetysa@cipla.com or telephone 080 222 6662 (toll free).

4.9 Overdose

The most frequent signs of overdosage include gastrointestinal complications and renovascular adverse events.

In the event of overdosage, the usual supportive measures should be employed. The unabsorbed material should be removed from the gut, patients should be clinically monitored and if necessary, supportive therapy should be given.

Haemodialysis is not effective in ETIFLAM overdosage treatment, and it is not known whether peritoneal dialysis is effective.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: A 3.1 Anti-rheumatics (anti-inflammatory agents).

ATC code: M01 AH05

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

5.2 Pharmacokinetic properties

Absorption

After oral administration, etoricoxib is absorbed with a mean oral bioavailability of approximately 100 %. Etoricoxib peak plasma concentration (geometric mean C_{max}) of 3,6 µg/mL was observed

after approximately 1 hour (t_{max}) when 120 mg daily doses were administered to adults under fasted conditions. The pharmacokinetics of etoricoxib are linear over clinical dose range.

Food (a standard meal) did not have a significant clinical effect on the extent or rate of absorption of etoricoxib when 120 mg doses were administered.

No major differences in pharmacokinetics were observed when etoricoxib was administered with or without antacids in healthy adults (40 - 65 years of age), namely, magnesium / aluminium hydroxide or calcium carbonate (approximately 50 mEq acid neutralising capacity) as the AUC was found to be comparable while C_{max} was well within 20 %.

Distribution

Etoricoxib plasma protein binding is approximately 92 % over concentrations of 0,05 to 5 µg/mL in humans. At steady state, the volume of distribution (V_{dss}) is approximately 120 L.

Etoricoxib crosses the placenta and the blood-brain barrier.

Biotransformation

Etoricoxib undergoes hepatic metabolism predominantly, with less than 1 % of the dose recovered in the urine as the parent drug. Five metabolites have been identified in humans.

Etoricoxib is mainly metabolised by cytochrome P450 enzymes to form the 6'-hydroxymethyl derivative which undergoes oxidation to form the principal metabolite 6'-carboxylic acid derivative. The major metabolites either have no measurable activity or act as weak inhibitors of COX-2.

Elimination

Following a 25 mg single dose intravenous administration of radio-labelled etoricoxib, 70 % radioactivity was recovered in the urine and 20 % in the faeces, mainly as metabolites. Afterwards, plasma and urine were collected for 7 days while stool was collected for 10 days. Less than 2 % was recovered as unchanged drug.

Elimination of etoricoxib is almost exclusively through metabolism followed by renal excretion. Steady state concentrations are reached after 7 days of once daily administrations of 120 mg, with an accumulation ratio of approximately 2, which is nearly equivalent to an accumulation half-life of approximately 22 hours. The plasma clearance is approximately 50 mL/min.

Pharmacokinetics in special populations

Elderly

In elderly patients (65 years and older) with normal renal function, no pharmacokinetic differences were observed. However, the incidence of adverse events was higher in the elderly.

Patients with hepatic impairment

Etoricoxib exposure (AUC) was approximately 16 % higher in patients with mild hepatic impairment (Child-Pugh score 5 to 6) when compared to healthy patients that received the same treatment regimen of 60 mg once daily for 21 days.

Patients with moderate hepatic impairment (Child-Pugh score greater than 9) administered with etoricoxib 60 mg on every other day for 21 days showed similar exposure (AUC) to healthy patients that were administered with daily doses of 60 mg for 21 days.

No data are available in patients with severe hepatic impairment (Child-Pugh score 7 to 9) (see **section 4.3** and **4.2**).

Patients with renal impairment

No significant pharmacokinetic differences were observed when a single dose of etoricoxib 120 mg was administered to patients with moderate (creatinine clearance 30 to 50 mL/min) to severe (creatinine clearance less than 30 mL/min) renal insufficiency or in patients with end-stage renal disease on haemodialysis. Haemodialysis contributed negligibly to elimination (dialysis clearance approximately 50 mL/min).

Paediatrics

Etoricoxib has not been studied in patients under 12 years of age. Safety and efficacy of ETIFLAM have not been established in paediatric and adolescent patients.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Core Tablet

Anhydrous calcium hydrogen phosphate

Croscarmellose sodium

Magnesium stearate

Microcrystalline cellulose

Film coated Tablet

Opadry II white 39K580004 (ETIFLAM 60)

Opadry II green 39K510004 (ETIFLAM 90 and ETIFLAM 120)

Composition of the film-coat (Opadry)

Hypromellose 15 mPas (E464)

Hypromellose 50 mPas (E464)

Lactose monohydrate

Titanium dioxide (E171)

Triacetin

*Iron Oxide yellow (E172)

*Indigo carmine (E132)

* Only applicable for ETIFLAM 90 and ETIFLAM 120

6.2 Incompatibilities

Not applicable

6.3 Shelf life

24 months

6.4 Special precautions for storage

Store at or below 30 °C. Store in the original package. Keep well closed.

6.5 Nature and contents of container

ETIFLAM film-coated tablets are packed in:

- Packs of 7's in Alu/Alu blisters that are placed into an outer cardboard carton.

- Packs of 10's in Alu/Alu blisters that are placed into an outer cardboard carton.
- Packs of 30's in Alu/Alu blisters that are placed into an outer cardboard carton or in white HDPE bottles fitted with white child-resistant caps embossed with the instruction "TO OPEN PUSH DOWN AND TURN & CLOSE TIGHTLY". The 30's HDPE packs contain a 2 g silica gel desiccant.
- Packs of 90's in white HDPE bottles fitted with white child-resistant caps embossed with the instruction "TO OPEN PUSH DOWN AND TURN & CLOSE TIGHTLY. The 90's HDPE packs contain a 1 g silica gel desiccant.
- The silica gel desiccant is made from a non-woven fabric bag and heat sealed along the edges with the manufacturer's details printed in blue ink.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

No special requirements

7. HOLDER OF CERTIFICATE OF REGISTRATION

CIPLA MEDPRO (PTY) LTD.

Building 9

Parc du Cap

Mispel Street

Bellville

7530

Customer Care: 080 222 6662

8. REGISTRATION NUMBER(S)

ETIFLAM 60: 50/3.1/0816.813

ETIFLAM 90: 50/3.1/0817.814

ETIFLAM 120: 50/3.1/0818.815

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

09 June 2020

10. DATE OF REVISION OF THE TEXT

13 July 2023