SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF DRUG PRODUCT

Etoget (Etoricoxib) Tablets 60mg

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains:
Etoricoxib 60mg

3. PHARMACEUTICAL FORM

White colored, round shaped, biconvex film coated tablet engraved GP on one side and plain on other side

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

Etoget (Etoricoxib) Tablets is indicated for:

- Symptomatic relief of Osteoarthritis (OA) and rheumatoid arthritis (RA)
- Management of ankylosing spondylitis (AS)
- Treatment of acute gouty arthritis
- 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

4.2 Posology and method of administration

Osteoarthritis:
The recommended dose is 30mg or 60mg once daily. The dose should not exceed 60 mg daily.

Rheumatoid Arthritis & Ankylosing Spondylitis
The recommended dose is 60mg or 90mg once daily. The dose should not exceed 90 mg daily.

Acute Gouty Arthritis
The recommended dose is 120mg once daily. Etoricoxib should not exceed 120 mg daily, limited to a maximum of 8 days treatment.

Post-Operative Dental Surgery Pain
The recommended dose is 90mg once daily. It should not exceed 90mg daily, limited to a maximum of 3 days.

Elderly patients
No dosage adjustment is necessary for elderly patients. As with other drugs, caution should be exercised in elderly patients.

Patients with renal impairment
No dosage adjustment is necessary for patients with creatinine clearance ≥30 ml/min. The use of Etoricoxib in patients with creatinine clearance <30 ml/min is contra-indicated.

Pediatric population
Etoricoxib is contra-indicated in children and adolescents under 16 years of age.

Hepatic Impairment
Regardless of indication, in patients with mild hepatic dysfunction (Child-Pugh score 5-6) a dose of 60mg once daily should not be exceeded. In patients with moderate hepatic dysfunction (Child-Pugh score 7-9) regardless of indication, the dose of 30mg once daily should not be exceeded.

4.3 Contra-indications

Etoricoxib is contraindicated in:

- Hypersensitivity to active substance or to any of the excipient of the product.
- Active peptic ulceration or active gastrointestinal (GI) bleeding.
- Patients who have experienced bronchospasm, acute rhinitis, nasal polyps, angioneurotic oedema, urticaria, or allergic-type reactions after taking acetylsalicylic acid or NSAIDs including COX-2 (cyclooxygenase-2) inhibitors.
- Severe hepatic dysfunction (serum albumin <25 g/L or Child-Pugh score ≥10).
- Estimated renal creatinine clearance < 30mL/min.
- Children and adolescents under 16 years of age.
- Inflammatory bowel disease.
- Congestive heart failure (NYHA II-IV).

- Patients with hypertension whose blood pressure is persistently elevated above 140/90mmHg and has not been adequately controlled.
- Established ischemic heart disease, peripheral arterial disease and/or cerebrovascular disease.
- Pregnancy and lactation

4.4 Special warnings and special precautions for use

Gastrointestinal effects
Caution is advised with treatment of patients most at risk of developing a gastrointestinal complication with NSAIDs; the elderly, patients using any other NSAID or acetylsalicylic acid concomitantly or patients with a prior history of gastrointestinal disease, such as ulceration and GI bleeding.

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

Aspirin substitution
COX-2 selective inhibitors are not a substitute for acetylsalicylic acid for prophylaxis of cardiovascular thrombo-embolic diseases because of their lack of antiplatelet effect. Therefore, antiplatelet therapies should not be discontinued.

Renal effects
In compromised renal perfusion, administration of Etoricoxib may cause a reduction in prostaglandin formation and, secondarily, in renal blood flow and thereby impair renal function. Monitoring of renal function in such patients should be considered.

Fluid retention, edema and hypertension
Fluid retention, edema and hypertension have been observed in patients taking Etoricoxib. All Nonsteroidal Anti-inflammatory Drugs (NSAIDs), including Etoricoxib, 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 edema from any other reason. If blood pressure raises significantly, alternative treatment should be considered.

Hepatic effects
Patients should be monitored with signs and symptoms of liver dysfunction, or with abnormal liver function test. If signs of hepatic insufficiency occur, or if persistently abnormal liver function tests (three times the upper limit of normal) are detected, Etoricoxib should be discontinued.

Hypersensitivity
Etoricoxib should be used with caution in patients who have previously experienced acute asthmatic attacks, urticaria, or rhinitis precipitated by salicylates or non-selective cyclooxygenase inhibitors.

General
Some selective COX-2 inhibitors have been associated with an increased risk of skin reactions in patients with a history of any drug allergy. Etoricoxib should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity.
Caution should be used when initiating treatment with Etoricoxib in patients with considerable dehydration. It is advisable to rehydrate patients prior to starting therapy with Etoricoxib.

4.5 Interaction with other medicaments and other forms of interaction

Oral anticoagulants
Patients receiving chronic warfarin therapy, the administration of Etoricoxib 120mg daily is associated with an increase in prothrombin time International Normalized Ratio (INR). Therefore, patient receiving oral anticoagulants should be closely monitored for their prothrombin time INR.

Diuretics, ACE inhibitors and Angiotensin II antagonists
In patients with compromised renal function the co-administration of an ACE inhibitor or Angiotensin II antagonist and agents that inhibit cyclo-oxygenase may result in further deterioration of renal function, including possible acute renal failure, which is usually reversible. Therefore, the combination should be administered with caution especially in the elderly.

Acetylsalicylic Acid
Concomitant administration of low-dose acetylsalicylic acid with Etoricoxib may result in an increased rate of GI ulceration or other complications compared to use of Etoricoxib alone.

Ciclosporin and Tacrolimus
Co-administration of Ciclosporin or Tacrolimus with any NSAID may increase the nephrotoxic effect of Ciclosporin or Tacrolimus.

Lithium
NSAIDs decrease lithium renal excretion and therefore increase lithium plasma levels. If necessary, monitor blood lithium closely and adjust the lithium dosage while the combination is being taken and when the NSAID is withdrawn.

Methotrexate
Adequate monitoring for methotrexate-related toxicity is recommended when Etoricoxib and methotrexate are administered concomitantly.

Oral contraceptives
Etoricoxib given concomitantly with oral contraceptive containing ethinyl estradiol and norethindrone increase the steady state AUC of ethinyl estradiol. This increase in concentration should be considered when selecting an appropriate oral contraceptive for use with Etoricoxib.

Hormone Replacement Therapy (HRT)
Administration of Etoricoxib with hormone replacement therapy increases the mean steady state AUC of unconjugated estrone, equilin, and 17-ß-estradiol. These increase in oestrogenic concentration should be taken into consideration when selecting post-menopausal hormone therapy for use with Etoricoxib.

Digoxin
Co-administration of Etoricoxib with digoxin, increase digoxin C_{max}. Therefore, patients at high risk of digoxin toxicity should be monitored when Etoricoxib and digoxin are administered concomitantly.

Sulfotransferases
Caution should be considered when administering Etoricoxib concurrently with other drugs primarily metabolized by human sulfotransferases (e.g., oral salbutamol and minoxidil).

Rifampicin
Co-administration of Etoricoxib with rifampicin, decrease Etoricoxib plasma concentrations. This interaction may result in recurrence of symptoms when Etoricoxib is co-administered with rifampicin.

4.6 Use in Pregnancy and Lactation

Pregnancy

Etoricoxib is contraindicated in pregnancy. If a woman becomes pregnant during treatment, Etoricoxib must be discontinued.

Nursing Mothers

Women who use Etoricoxib must not breast feed.

Fertility

The use of Etoricoxib, as with any active substance known to inhibit COX-2, is not recommended in women attempting to conceive.

4.7 Undesirable effect

Common

Alveolar osteitis, edema/fluid retention, dizziness, headache, palpitations, arrhythmia, hypertension, bronchospasm, constipation, flatulence, gastritis, acid reflux, diarrhea, dyspepsia, epigastric discomfort, nausea, vomiting, esophagitis, oral ulcer, ALT increased, AST increased, ecchymosis, asthenia/fatigue and flu-like disease.

Uncommon

Gastroenteritis, upper respiratory infection, urinary tract infection, anemia, leukopenia, thrombocytopenia, hypersensitivity, increase or decrease appetite, weight gain, anxiety, depression, mental acuity decreased, hallucinations, dysgeusia, insomnia, paresthaesia/hypaesthesia, somnolence, blurred vision, conjunctivitis, tinnitus, vertigo, atrial fibrillation, tachycardia, congestive heart failure, non-specific ECG changes, angina pectoris, myocardial infarction, flushing, cerebrovascular accident, transient ischemic attack, hypertensive crisis, vasculitis, cough, dyspnea, epistaxis, abdominal distention, bowel movement pattern change, constipation, dry mouth, gastroduodenal ulcer, peptic ulcer, irritable bowel syndrome, pancreatitis, facial edema, pruritus, rash, erythema, urticaria, muscular cramp/spasm, musculoskeletal pain/stiffness, proteinuria, serum creatinine increased, renal failure/renal insufficiency, chest pain, blood urea nitrogen increased, creatine phosphokinase increased, hyperkalemia and uric acid increased.

Rare

Angioedema/anaphylactic/anaphylactoid reactions including shock, confusion, restlessness, hepatitis, hepatic failure, jaundice, Stevens-Johnson syndrome, toxic epidermal necrolysis, fixed drug eruption and blood sodium decreased.

4.8 Overdose

Symptoms:

The most frequently observed adverse experiences are consistent with the safety profile for Etoricoxib (e.g., gastrointestinal events, cardiorenal events).

Treatment:

In the event of overdose, it is reasonable to employ the usual supportive measures, e.g., remove unabsorbed material from the GI tract, employ clinical monitoring and institute supportive therapy, if required. Etoricoxib is not dialyzable

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic Group: Anti-inflammatory and antirheumatic products, non-steroids, coxibs,
ATC code: M01AH05

Mechanism of Action

Etoricoxib is an oral, selective cyclo-oxygenase-2 (COX-2) inhibitor. Etoricoxib produced dose-dependent inhibition of COX-2 without inhibition of COX-1 at doses up to 150mg daily. Etoricoxib does not inhibit gastric prostaglandin synthesis and has no effect on platelet function.
Selective inhibition of COX-2 by Etoricoxib decreases the synthesis of prostanoid mediators of pain, inflammation, and fever with decreased potential GI toxicity and effects on platelet aggregation.

5.2 Pharmacokinetic properties

Absorption

Etoricoxib is well absorbed from the gastrointestinal tract after oral doses. The absolute bioavailability is 100%. Peak plasma concentrations are reached in about 1 hour in fasted adults.
Effect of food: Food delays absorption by about 2 hours, although it has no effect on the extent of absorption.

Distribution

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

Metabolism

Etoricoxib is extensively metabolized with less than 1% of a dose recovered in the 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 oxidized to the 6'-carboxylic acid derivative, the major metabolite. Both are inactive or only weak cyclo-oxygenase-2 (COX-2) inhibitors.

Excretion

Excretion is mainly via the urine (70%) with only 20% of a dose appearing in the feces, mostly as metabolites. Less than 2% is recovered as unchanged drug. Steady state concentrations of Etoricoxib are reached within seven days of once daily administration of 120mg. At steady state the half-life of Etoricoxib is about 22hours.

Special Populations

Hepatic Impairment

Patients with mild hepatic dysfunction (Child-Pugh score 5-6) administered etoricoxib 60mg once daily has an approximately 16% higher mean AUC as compared to healthy subjects given the same regimen. Patients with moderate hepatic dysfunction (Child-Pugh score 7-9) administered etoricoxib 60mg every other day has similar mean AUC to the healthy subjects given etoricoxib 60mg once daily.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

- Avicel PH-101
- Dicalcium Phosphate Anhydrous (DiCafos)

- Croscarmellose Sodium
- Magnesium Stearate
- Opadry II White 85F18422

6.2 Incompatibilities

Not applicable.

6.3 Shelf-life

2 years
The expiration date refers to the product correctly stored in the required conditions.

6.4 Special precautions for storage

- Do not store above 30°C.
- Protect from sunlight and moisture.
- The expiry date refers to the product correctly stored at the required conditions.

6.5 Nature and contents of container

Etoget (Etoricoxib) Tablets 60mg are available in Alu-Alu blister pack of 30's (3×10's) in a unit carton along with package insert

6.6 Instructions for use/handling

- Keep out of reach of children.
- To be sold on prescription of a registered medical practitioner only.

7. MARKETING AUTHORISATION HOLDER

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APPLICANT:
GETZ PHARMA NIGERIA LIMITED
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OFF ADEYEMO ALAKIJA STREET
IKEJA GRA, LAGOS.

8. PRODUCT REGISTRATION NUMBER

007134 – EX

9. DATE OF PRODUCT REGISTRATION ISSUED

May 30th, 2018