(L)297mm

(W)210mm

pharmaniaga®

Rabirox

Celecoxib 200mg
Celecoxib 400mg

COMPOSITION
Rabirox Capsule 200 mg
Each capsule contains 200 mg of celecoxib

Rabirox Capsule 400 mg
Each capsule contains 400 mg of celecoxib

DESCRIPTION
Rabirox Capsule 200 mg
White to off white granules in white opaque hard gelatin capsule size '2'.

Rabirox Capsule 400 mg
White to off white granules in white opaque hard gelatin capsule size '0'.

PHARMACODYNAMICS
Pharmacotherapeutic group: M01AH Coxibs

The mechanism of action of celecoxib is via inhibition of prostaglandin synthesis primarily by inhibition of cyclooxygenase 2 (COX-2). At therapeutic concentrations in humans, celecoxib does not inhibit cyclooxygenase 1 (COX-1). COX-2 is induced in response to inflammatory stimuli. This leads to the synthesis and accumulation of inflammatory prostanoids, in particular prostaglandin E2, causing inflammation, edema and pain. Celecoxib acts as an anti-inflammatory, analgesic, and antipyretic agent by blocking the production of inflammatory prostanoids via COX-2 inhibition. Celecoxib also reduced the incidence and multiplicity of tumors.

Celecoxib has a very low affinity for the constitutively expressed COX-1 enzyme. Consequently, at therapeutic doses celecoxib has no effect on prostanoids synthesized by activation of COX-1 thereby not interfering with normal COX-1 related physiological process in tissues, particularly the stomach, intestine and platelets.

PHARMACOKINETICS
Absorption
When given under fasting conditions celecoxib is well absorbed reaching peak plasma concentrations after approximately 2-3 hours. Oral bioavailability from capsules is about 99% relative to administration in suspension (optimally available oral dosage form). Under fasting conditions, both peak plasma levels (C_{max}) and area under the curve (AUC) are roughly dose proportional up to 200 mg twice daily; at higher doses there are less than proportional increases in C_{max} and AUC.

Distribution
Plasma protein binding, which is concentration independent, is about 97% at therapeutic plasma concentration and the drug is not preferential bound to erythrocytes in the blood.

Metabolism
Celecoxib metabolism is primarily mediated via cytochrome P450 2C9. Three metabolites, inactive as COX-1 or COX-2 inhibitors, have been identified in human plasma: a primary alcohol, the corresponding carboxylic acid and its glucuronide conjugate.

Cytochrome P450 2C9 activity is reduced in individuals with genetic polymorphisms that lead to reduced enzyme activity, such as those homozygous for the CYP2C9*3 polymorphism.

Patients who are known, or suspected to be CYP2C9 poor metabolizers based on previous history/experience with other CYP2C9 substrates should be administered celecoxib with caution.

Elimination
Elimination of celecoxib is mostly by hepatic metabolism with less than 1% of the dose excreted unchanged in urine. Elimination half-life is 8-12 hours and the rate of clearance is about 500ml/min. Steady-state plasma concentrations are reached before day 5 of treatment. The inter-subject variability on the main pharmacokinetic parameters (AUC, C_{max}, elimination half-life) is about 30%. The mean steady-state volume of distribution is about 500 L/70 kg in young healthy adults indicating wide distribution of celecoxib into tissue. Celecoxib crosses the blood/brain barrier.

Food Effects
Dosing with food (high fat meal) delays absorption of celecoxib resulting in a T_{max} of about 4 hours and increases bioavailability about 20%.

INDICATION
- For the management of acute pain in adults and for the treatment of primary dysmenorrhea.
- Relief of the acute and chronic pain and inflammation of rheumatoid arthritis and osteoarthritis.
- Relief of signs and symptoms of ankylosing spondylitis.
- For the management of low back pain (200mg only).

RECOMMENDED DOSAGE
Celecoxib capsules can be taken with or without food.
Given the association between cardiovascular risk and exposure to COX-2 inhibitor, doctors are advised to use the lowest effective dose for the shortest possible duration of treatment.

Adults
Symptomatic Treatment of Osteoarthritis (OA): The recommended dose of celecoxib is 200mg administrated as a single dose.

Symptomatic treatment of Rheumatoid Arthritis (RA): The recommended dose of celecoxib is 200mg twice per day.

Ankylosing Spondylitis (AS): The recommended dose of celecoxib is 200 mg administered as a single dose. Some patients may benefit from total daily dose of 400 mg.

Management Acute Pain: The recommended dose of celecoxib is 400 mg, initially, followed by an additional 200 mg dose, if needed on the first day. On subsequent days, the recommended dose is 200 mg twice daily, as needed.

Treatment of Primary Dysmenorrhea: The recommended dose of celecoxib is 400 mg, initially, followed by an additional 200 mg dose, if needed on the first day. On subsequent days, the recommended dose is 200 mg twice daily, as needed.

Low Back Pain (LBP): Usual dosage for adults is 200mg once daily.

Elderly: No dosage adjustment is generally necessary. However, for elderly patients with a lower than average body weight (<50 kg), it is advisable to initiate therapy at the lowest recommended dose.

Hepatic impairment: No dosage adjustment is necessary in patients with mild hepatic impairment (Child-Pugh Class A). Introduce celecoxib at half the recommended dose in arthritis or pain patients with moderate hepatic impairment (Child-Pugh Class B).

Patients with severe hepatic impairment (Child-Pugh Class C) have not been studied.

Renal impairment: No dosage adjustment is necessary in patients with mild or moderate renal impairment.

Children: Celecoxib is not indicated for use in children.

CYP2C9 Poor Metabolizers: Patients who are known or suspected to be CYP2C9 poor metabolizers based on genotyping or previous history/experience with other CYP2C9 substrates should be administered celecoxib with caution as the risk of dose-dependent adverse effects is increased. Consider reducing the dose to half the lowest recommended dose.

MODE OF ADMINISTRATION
Oral

CONTRAINDICATIONS
Celecoxib is contraindicated in:
- Patients with known hypersensitivity to celecoxib or any other ingredient of the product.
- Patients with known sulfonamide hypersensitivity.
- Patients who have experienced asthma, urticaria or allergic-type reactions after taking acetylsalicylic acid (ASA [aspirin]) or other non-steroidal anti -inflammatory drugs (NSAIDs), including other cyclooxygenase-2 (COX-2) specific inhibitors).
- Treatment of peri-operative pain in the setting of coronary artery bypass Graff (CABG) surgery.
- Patients who have established cardiovascular disease (ischemic heart disease and stroke).
- Patients with hypertension (high blood pressure) whose blood pressure is not under control.
- Active peptic ulceration or gastrointestinal (GI) bleeding.
- Severe hepatic dysfunction (serum albumin <25 g/l or Child-Pugh score =10).
- Patients with estimated creatinine clearance <30 ml/min.
- Inflammatory bowel disease.
- Congestive heart failure (NYHA II-IV).
- Established peripheral arterial disease and/or cerebrovascular disease.

WARNINGS AND PRECAUTIONS

WARNING

RISK OF GI ULCERATION, BLEEDING AND PERFORATION WITH NSAID

Serious GI toxicity such as bleeding, ulceration and perforation can occur at any time, with or without warning symptoms, in patients treated with NSAID therapy. Although minor upper GI Problems (e.g. dyspepsia) are common, usually developing early in therapy, prescribers should remain alert for ulceration and bleeding in patients treated with NSAIDs even in the absence of previous GI tract symptoms.

Studies to date have not identified any subset of patients not a risk of developing peptic ulceration and bleeding. Patients with prior history of serious GI events and other risk factors associated with peptic ulcer disease (e.g. alcoholism, smoking, and corticosteroid therapy) are at increased risk. Elderly or debilitated patients seem to tolerate ulceration or bleeding less than other individuals and account for most spontaneous reports for fatal GI events.

Warning to prescriber when prescribing COX-2 Inhibitors to patients with risk factors of heart disease, hypertension (high blood pressure), hyperlipidemia, diabetes, smoking patient and patient with peripheral arterial disease.

Cardiovascular Effects
Cardiovascular Thrombotic Events: Celecoxib may cause an increased risk of serious cardiovascular (CV) thrombotic events, myocardial infarction (MI), and stroke, which can be fatal. All NSAIDs may have similar risk. This risk may increase with dose, duration of use and baseline cardiovascular risk factors. Patients with known medical history of cardiovascular disease may be at greater risk. To minimize the potential risk for an adverse cardiovascular event in patients treated with celecoxib, the lowest effective dose should be used for the shortest duration possible. Physicians and patients should remain alert for the development of such events, even in the absence of previous cardiovascular symptoms. Patients should be informed about the signs and symptoms of serious cardiovascular toxicity and the steps to take if they occur.

Administration COX-2 selective NSAID for the treatment of pain in the first 10-14 days following CABG surgery found an increased incidence of myocardial infarction and stroke.

Celecoxib is not substitute for acetylsalicylic acid of prophylaxis of cardiovascular thrombo-embolic diseases because of the lack of effect on platelet function. Because Celecoxib does not inhibit platelet aggregation, anti-platelet therapies (e.g., acetylsalicylic acid) should not be discontinued.

Hypertension: As with all NSAIDS, celecoxib can lead to the onset of new hypertension or worsening of pre-existing hypertension, either of which may contribute to the increased incidence of cardiovascular events. Patients taking angiotensin converting enzyme (ACE) inhibitors, thiazide diuretics or loop diuretics may have impaired response to these therapies when taking NSAIDs. NSAIDs, including celecoxib, should be used with caution in patients with hypertension. Blood pressure should be monitored closely during the initiation of therapy with celecoxib and throughout the course of therapy.

Fluid Retention and Edema: As with other drugs known to inhibit prostaglandin synthesis, fluid retention and edema have been observed in some patients taking celecoxib. Therefore, patients with pre-existing congestive heart failure or hypertension should be closely monitored. Celecoxib should be used with caution in patients with compromised cardiac function, pre-existing edema, or other conditions predisposing to, or worsened by, fluid retention including those taking diuretic treatment or otherwise at risk of hypovolemia.

Gastrointestinal (GI) Effects
Upper and lower GI perforations, ulcer or bleeds have occurred in patients treated with celecoxib. These serious adverse events can occur at any time, with or without warning symptoms, in patients treated with celecoxib. Patients most at risk of developing these types of GI complications with NSAIDs are the elderly, patients with cardiovascular disease, patients using concomitant aspirin, glucocorticoids, or other NSAIDs, patients using alcohol or patients with a prior history of, or active, GI disease, such as ulceration, GI bleeding or inflammatory conditions. Other factors that increase the risk of GI bleeding in patients treated with NSAIDs include longer duration of NSAID therapy; concomitant use of oral corticosteroids, aspirin, anticoagulants; or selective serotonin reuptake inhibitors (SSRIs); smoking; use of alcohol; older age; and poor general health status. Most spontaneous reports of fatal GI events have been in elderly or debilitated patients.

Strategies to minimize the GI Risks in NSAID-treated patients:
- Use the lowest effective dosage for the shortest possible duration.
- Avoid administration of more than one NSAID at one time.
- Avoid use in patients at higher risk unless benefits are expected to outweigh the increased risk of bleeding. For such patients, as well as those with active GI bleeding, consider alternate therapies other than NSAIDs.
- Remain alert for signs and symptoms of GI ulceration and bleeding during NSAID therapy.
- If a serious GI adverse event is suspected, promptly initiate evaluation and treatment, and discontinue celecoxib until a serious GI adverse event is ruled out.
- In the setting of concomitant use of low-dose aspirin for cardiac prophylaxis, monitor patients more closely for evidence of GI bleeding.

Renals Effects
NSAIDs including celecoxib may cause renal toxicity. Patients at greatest risk for renal toxicity are those with impaired renal function, heart failure, liver dysfunction, and the elderly. Such patients should be carefully monitored while receiving treatment with celecoxib.

Caution should be used when initiating treatment in patients with dehydration. It is advisable to rehydrate patients first and then start therapy with celecoxib.

Advanced Renal Disease
Renal functions should be closely monitored in patients with advanced renal disease who are administered celecoxib.

Anaphylactoid Reactions
As with NSAIDs in general, anaphylactoid reactions have occurred in patients exposed to celecoxib.

Serious Skin Reactions
Serious skin reactions, some of them fatal, including exfoliative dermatitis, Stevens-Johnson syndrome, and toxic epidermal necrolysis, have been reported very rarely in association with the use of celecoxib. Patients appear to be at highest risk for these events early in the course of therapy, the onset of the event occurring in the majority of cases within the first month of treatment. Celecoxib should be discontinued at the first appearance of skin rash, mucosal lesions, or and other sign of hypersensitivity.

Hepatic Effects
Patients with severe hepatic impairment (Child-Pugh Class C) have not been studied. The use of celecoxib in patients with severe hepatic impairment is not recommended. Celecoxib should be used with caution when treating patients with moderate hepatic impairment (Child-Pugh Class B),and initiated at half the recommended dose.

attn	customer **Pharmaniaga Manufacturing Berhad**	date **07.06.2022**
1 colours	process colours: **Black**	**Please Chop & Sign For Approval**
size (L)**297 x** (W)**210mm**	material **60gm simili**	
description **Rabirox Insert - Front (PRP 0553.2/ PRP 0554.2 030622)**		
FocusPrint SDN BHD	t: 603-8766 6030 f: 603-8766 6033 (Factory) website: www.focusprint.com.my	
artwork prepared by: cynthia yap	email: graphic@focusprint.info (graphic Dept)	**date:**

ARTWORK LOG

Revision no.	Date	Reason for Change
01	07.06.2022	- New artwork and amend wording on second page.
02	07.06.2022	- Add bracket to co. no. and amend Jun to June.

IMPORTANT ! **Please note that this colour print is for visual purpose only. Output colour might differ in actual production.**

(L)297mm

(W)210mm

Rare cases of severe hepatic reactions, including fulminant hepatitis (some with fatal outcome), liver necrosis, and hepatic failure (some with fatal outcome or requiring liver transplant), have been reported with celecoxib.

A patient with symptoms and/or signs of liver dysfunction, or in whom an abnormal liver function test has occurred, should be monitored carefully for evidence of the development of a more severe hepatic reaction while on therapy with celecoxib.

Use with Oral Anticoagulants
The concomitant use of NSAIDs with oral anticoagulants increases the risk of bleeding and should be given with caution. Oral anticoagulants include warfarin/coumarin-type and novel oral anticoagulants (e.g. apixaban, dabigatran, and rivaroxaban). In patients on concurrent therapy with warfarin or similar agents, serious bleeding events, some of them fatal, have been reported. Because increases in prothrombin time (INR) have been reported, anticoagulation/INR should be monitored in patients taking a warfarin/coumarin-type anticoagulant after initiating treatment with celecoxib or changing the dose.

General
By reducing inflammation, celecoxib may diminish the utility of diagnostic signs, such as fever, in detecting infections.
The concomitant use of celecoxib and a non-aspirin NSAID should be avoided.

CYP 2D6 inhibition
Celecoxib inhibits CYP2D6. Although it is not a strong inhibitor of this enzyme, a dose reduction may be necessary for individually dose-titrated drugs that are metabolized by CYP2D6.

CYP2C9 poor metabolisers
Patients known to be CYP2C9 poor metabolisers should be treated with caution.

EFFECTS ON THE ABILITY TO DRIVE AND USE MACHINES
The effect of celecoxib on ability to drive or use machinery has not been studied, but based on its pharmacodynamic properties and overall safety profile it is unlikely to have an effect.

INTERACTIONS WITH OTHER MEDICAMENTS
General: Celecoxib metabolism is predominantly mediated via cytochrome P450 (CYP) 2C9 in the liver. Patients who are known or suspected to be poor CYP2C9 metabolizers based on previous history/experience with other CYP2C9 substrates should be administered celecoxib with caution as they may have abnormally high plasma levels due to reduced metabolic clearance. Consider starting treatment at half the lowest recommended dose.

Concomitant administration of celecoxib with inhibitors of CYP2C9 can lead to increases in plasma concentrations of celecoxib. Therefore, a dose reduction of celecoxib may be necessary when celecoxib is co-administered with CYP2C9 inhibitors.

Concomitant administration of celecoxib with inducers of CYP2C9, such as rifampicin, carbazepine and barbiturates can lead to decreased in plasma concentrations of celecoxib.

Celecoxib, although not a substrate, is an inhibitor of CYP2D6. Therefore, there is potential for an in vivo drug interaction with drugs that are metabolized by CYP2D6.

Drug-specific
Interaction of celecoxib with warfarin or similar agents: (See Warnings and Precautions for Use with Oral Anticoagulants).

Lithium: When receiving lithium together with celecoxib, lithium plasma levels increased approximately 17%. Therefore, patients on lithium treatment should be closely monitored when celecoxib is introduced or withdrawn.

Aspirin: Celecoxib does not interfere with the anti-platelet effect of low-dose aspirin. Because of its lack of platelet effects, celecoxib is not a substitute for aspirin in the prophylactic treatment of cardiovascular disease.

Anti-hypertensives including Angiotensin-converting enzyme inhibitors (ACEIs), Angiotensin II antagonist (also known as angiotensin receptor blockers, ARBs), diuretics and beta-blockers: Inhibition of prostaglandins may diminish the effect of anti-hypertensives including (ACEIs), and/or ARBs, diuretics and beta-blockers. This interaction should be given consideration in patients taking celecoxib concomitantly with ACEIs and/or ARBs, diuretics and beta-blockers.

In patients who are elderly, volume depleted (including those on diuretic therapy), or with compromised renal function, co-administration of NSAIDs, including selective COX-2 inhibitors, with ACE inhibitors, angiotensin II antagonists or diuretics, may result in deterioration of renal function, including possible acute renal failure. These effects are usually reversible. Therefore, the concomitant administration of these drugs should be done with caution. Patients should be adequately hydrated and the clinical need to monitor the renal function should be assessed at the beginning of the concomitant treatment and periodically thereafter.

Lisinopril: Approximately half of patients who received the ACE inhibitor, lisinopril, in combination with celecoxib were unresponsive to lisinopril at the final clinic visit, compared to under one third of patients who received lisinopril in combination with placebo; and this difference was statistically significant.

Cyclosporine: Because of their effect on renal prostaglandins, NSAIDs may increase the risk of nephrotoxicity with cyclosporine.

Fluconazole and ketoconazole: Since celecoxib is predominantly metabolized by CYP2C9 it should be used at half the recommended dose in patients receiving fluconazole. Concomitant use of 200 mg single dose of celecoxib and 200 mg once daily of fluconazole, a potent CYP2C9 inhibitor, resulted in a mean increase in celecoxib C_{max} of 60% and AUC of 130%. Ketonazole, a CYP3A4 inhibitor, showed no clinically relevant inhibition in the metabolism of celecoxib.

Dextromethorphan and metoprolol: Concomitant administration of celecoxib 200 mg twice daily resulted in a 2.6-fold and 1.5-fold increase in plasma concentration of dextromethorphan and metoprolol (CYP2D6 substrates), respectively. These increases are due to celecoxib inhibition to the CYP2D6 substrate metabolism via CYP2D6. Therefore, the dose of drugs as CYP2D6 substrate may need to be reduced when treatment with celecoxib is initiated or increased when treatment with celecoxib is terminated.

Diuretics: NSAIDs, in some patients, can reduce the natriuretic effect of furosemide and thiazides by inhibition of renal prostaglandin synthesis.

Methotrexate: No pharmacokinetic interactions have been observed when combining celecoxib and methotrexate.

Oral contraceptives: Celecoxib had no effects on the pharmacokinetics of a prototype combination oral contraceptive (1 mg norethindrone/0.035 mg ethinyl estradiol).

Other drugs: No interactions have been observed with celecoxib and antacids (aluminium and magnesium), omeprazole, glibenclamide (glyburide), phenytoin, or tolbutamine.

PREGNANCY AND LACTATION

Pregnancy
Celexocib, as with other drugs inhibiting prostaglandin synthesis, may cause uterine inertia and premature closure of the ductus arteriosus and should be avoided during the third trimester of pregnancy. Celecoxib should be used during pregnancy only if the potential benefit to the mother justifies the potential risk to the fetus.

Inhibition of prostaglandin synthesis might adversely affect pregnancy. There is an increased risk of spontaneous abortion after use of prostaglandin synthesis inhibitors in early pregnancy. Administration of prostaglandin synthesis inhibitors has been shown to result in increased pre and post implantation loss.

If used during second or third trimester of pregnancy, NSAIDs may cause fetal renal dysfunction which may result in reduction of amniotic fluid volume or oligohydramnios in severe cases. Such effects may occur shortly after treatment initiation and are usually reversible. Pregnant women on celecoxib should be closely monitored for amniotic fluid volume.

Lactation
Celecoxib is excreted in milk at concentrations similar to those in plasma. Administration of celecoxib to lactating women has shown very low transfer of celecoxib into breast milk. Because of the potential for adverse reactions in nursing infants from celecoxib, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the expected benefit of the drug to the mother.

ADVERSE EFFECTS / UNDESIRABLE EFFECTS
Adverse reactions are listed by system organ class and ranked by frequency in Table as below:

System Organ Class Frequency	**Adverse Drug Reaction**
Infections and infestations Common Uncommon	 Bronchitis, sinusitis, upper respiratory tract infection, urinary tract infection, ear infection, fungal infection Pharyngitis, rhinitis, Helicobacter infection, herpes zoster, erysipelas, wound infections, gingivitis, labyrinthitis, bacterial infection
Blood and lymphatic system disorders Uncommon Rare	 Anemia Thrombocytopenia
Immune system disorders Uncommon	 Hypersensitivity
Very rare	Anaphylactic reaction
Psychiatric disorders Common	 Insomnia
Uncommon	Anxiety, sleep disorder
Rare	Confusional state, hallucination
Nervous system disorders Common	 Dizziness
Uncommon	Hypertonia, somnolence, cerebral infarction
Very rare	Cerebral hemorrhage, meningitis aseptic, ageusia, anosmia
Eye Disorders Uncommon	 Vision blurred, conjunctival hemorrhage, vitreous floaters, conjunctivitis
Ear and labyrinth disorders Uncommon	 Tinnitus, hypoacusis
Cardiac disorders Common	 Myocardial infarction, angina pectoris
Uncommon	Palpitations, angina unstable, aortic valve incompetence, arteriosclerosis coronary artery, sinus bradycardia, ventricular hypertrophy.
Rare	Cardiac failure congestive, arrhythmia, tachycardia
Vascular disorders Common	 Hypertension (including aggravated hypertension)
Uncommon	Deep vein thrombosis, haematoma
Rare	Flushing
Very rare	Vasculitis
Respiratory, thoracic and mediastinal disorders Common	 Cough, dyspnoea
Uncommon	Dysphonia
Rare	Pulmonary embolism, pneumonitis
Gastrointestinal disorders Very common	 Diarrhea
Common	Vomiting, abdominal pain, dyspepsia, flatulence, dysphagia, irritable bowel syndrome, gastrooesophageal reflux disease, nausea, diverticulum
Uncommon	Gastric ulcer, tooth disorder, hemorrhoidal haemorrhage, frequent bowel movements, mouth ulceration, stomatitis
Rare Very rare	Duodenal ulcer, oesophageal ulcer, gastrointestinal hemorrhage Intestinal perforation, pancreatitis
Hepatobiliary disorders Uncommon	 Hepatic enzyme increased (include alanine aminotransferase increased and aspartate aminotransferase increased)
Rare	Hepatitis
Very rare	Hepatic failure, hepatitis fulminant, hepatic necrosis, cholestasis, hepatitis cholestatic, jaundice
Skin and subcutaneous tissue disorders Common	 Pruritus (includes pruritus generalized), rash
Uncommon	Urticaria, ecchymosis, dermatitis allergic
Rare	Angioedema, alopecia, photosensitivity reaction
Very rare	Dermatitis bullous, Stevens-Johnson syndrome, erythema multiforme, toxic epidermal necrolysis, drug reaction with eosinophilia and systemic symptoms (DRESS), acute generalized exanthematous pustulosis (AGEP), dermatitis exfoliative
General disorders and administrations site conditions Common	 Oedema, peripheral edema, blood creatinine increased, prostatic specific antigen increased, weight increased.
Uncommon	Face oedema, influenza-like illness, blood potassium increased, blood sodium increased, blood testosterone decreased, haematocrit decreased, haemoglobin increased, chest pain
Injury, poisoning and procedural conditions Uncommon	 Injury, foot fracture, lower limb fracture, fracture epicondylitis, tendon rupture
Neoplasms benign, malignant and unspecified Uncommon	 Lipoma
Musculoskeletal and connective tissue disorders Common	 Muscle spasms
Uncommon	Synovial cyst
Renal and urinary disorders Common	 Nephrolithiasis
Uncommon	Nocturia
Rare	Renal failure acute, hyponatremia
Very rare	Tubulointerstitial nephritis, nephrotic syndrome, glomerulonephritis minimal lesion
Reproductive system and breast disorders Common	 Vaginal haemorrhage, prostatitis, benign prostatic hyperplasia.
Uncommon	Ovarian cyst, menopausal symptoms, breast tenderness, dysmenorrhea
Rare	Menstrual disorder
Not known	Infertility female (female fertility decreased)

OVERDOSE AND TREATMENT
In the event of suspected overdose, appropriate supportive medical care should be provided. Dialysis is unlikely to be an efficient method of drug removal because of high protein binding of the drug.

STORAGE CONDITION
Store below 30°C.

SHELF LIFE
Product should not be used beyond the expiry date imprinted on the product packaging.

DOSAGE FORMS AND PACKAGING AVAILABLE
Alu/Aluminium blisters

Rabirox Capsule 200 mg:
In blisters of 100's (10 Alu-Alu blisters x 10 capsules) and 500's (50 Alu-Alu blisters x 10 capsules).

Rabirox Capsule 400 mg:
In blisters of 100's (10 Alu-Alu blisters x 10 capsules) and 500's (50 Alu-Alu blisters x 10 capsules).

Date of revision: 03rd June 2022

PRODUCT REGISTRATION HOLDER/MANUFACTURER:
PHARMANIAGA MANUFACTURING BERHAD (198001006232)
No. 11A, Jalan P/1, Kawasan Perusahaan Bangi,
43650 Bandar Baru Bangi, Selangor Darul Ehsan, Malaysia

PRP 0553.2/ PRP 0554.2 030622

attn	customer **Pharmaniaga Manufacturing Berhad**	date **07.06.2022**
1 colours	process colours: **Black**	**Please Chop & Sign For Approval**
size description	(L)**297 x** (W)**210mm** **Rabirox Insert - Back** **(PRP 0553.2/ PRP 0554.2 030622)**	material **60gm simili**
FocusPrint SDN BHD	t: 603-8766 6030 f: 603-8766 6033 (Factory) website: www.focusprint.com.my	
artwork prepared by: cynthia yap	email: graphic@focusprint.info (graphic Dept)	**date:**

IMPORTANT ! **Please note that this colour print is for visual purpose only. Output colour might differ in actual production.**

ARTWORK LOG

Revision no.	Date	Reason for Change
01	07.06.2022	- New artwork and amend wording on second page.
02	07.06.2022	- Add bracket to co. no. and amend Jun to June.