PELUBI® Tab.

Pelubiprofen 30mg

■ **COMPOSITION** : Each tablet contains

Pelubiprofen 30mg

■ **DESCRIPTION**

Lemon yellow circular tablet.

■ **INDICATIONS**

For relief of the signs and symptoms of osteoarthritis or lumbago.

■ **DOSAGE & ADMINISTRATION**

Adult : The recommended oral dose is 30mg three times per day after meals.

■ **PRECAUTIONS**

1. Warning

1) Patients who generally consume 3 or more alcohol-containing drinks per day should ask their clinician whether to use pelubiprofen or alternative analgesic antipyretics. Since this drug increases risk of GI bleeding in these patients.

2) Cardiovascular Risk : This drug may cause an increased risk of serious cardiovascular thrombotic events, myocardial infarction, and stroke, which can be fatal. All NSAIDs may have a similar risk. This risk may increase with duration of use. Patients with cardiovascular disease or risk factors for cardiovascular disease may be at greater risk.
Physicians and patients should remain alert for the development of such events, even in the absence of previous CV symptoms. Patients should be informed about the signs and/or symptoms of serious CV toxicity and the steps to take if they occur

3) Gastrointestinal Risk : NSAIDs, including this drug, cause an increased risk of serious gastrointestinal adverse events including bleeding, ulceration, and perforation of the stomach or intestines, which can be fatal. These events can occur at any time during use and without warning symptoms.
Elderly patients are at greater risk for serious gastrointestinal events.
With longer duration of use of NSAIDs, there is a trend for increasing the likelihood of developing a serious GI event at some time during the course of therapy. However, even short-term therapy is not without risk.
Physicians and patients should remain alert for signs and symptoms of GI ulceration and bleeding during pelubiprifen therapy and promptly initiate additional evaluation and treatment if a serious GI adverse event is sus pected. Use of NSAIDs could be discontinued as a treatment of serious GI event. This should include discontinuation of the NSAID until a serious GI adverse event is ruled out. For high-risk patients, alternate therapies that do not involve NSAIDs should be considered.

2. Contraindication

1) Patients with Peptic ulcer disease
2) Patients with severe hematological abnormalities
3) Patients with severe hepatic dysfunction.
4) Patients with severe renal dysfunction.
5) Patients with severe heart failure
6) Patients with severe Hypertension
7) Patients with known hypersensitivity to pelubiprofen.
8) Patients who have experienced asthma, urticaria, or allergic-type reactions after taking aspirin or other NSAIDs(Severe, rarely fatal, anaphylactic-like reactions to NSAIDs have been reported in such patients.).
9) Treatment of peri-operative pain in the setting of coronary artery bypass graft(CABG) surgery.
10) Lactation
11) PELUBI contains lactose and therefore should not be used in patients with rare hereditary problems of galactose intolerance, Lapp lactase deficiency or glucose-galactose malabsorption.

3. Caution

1) Patients with a prior history of peptic ulcer disease.
2) Patients with a prior history of haematological abnormalities
3) Patients with bleeding tendency (platelets function disorder may occur)
4) Patients with a prior history of hepatic dysfunction.
5) Patients with a prior history of renal dysfunction
6) Patients with heart dysfunction
7) Hypertension patients
8) Patients with a prior history of hypersensitivity
9) Patients with asthma
10) Patients with systemic lupus erythematosus (SLE) and mixed connective tissue disease (MCTD)
11) Patients with ulcerative colitis
12) Patients with crohn's disease
13) Geriatric and pediatric patients

4. Adverse reactions

636 patients have received pelubiprofen 30mg to 120mg per day, three times a day in clinical trials. Table 1 lists all adverse events, regardless of causality.

[Table 1] Adverse events occurring in clinical trials (%)

System/ Adverse event	30mg/ day (n=59)	60mg/ day (n=59)	90mg/ day (n=206)	120mg/ day (n=312)	System/ Adverse event	30mg/ day (n=59)	60mg/ day (n=59)	90mg/ day (n=206)	120mg/ day (n=312)
Gastrointestinal					Cardiovascular				
Nausea,Vomiting	1.7		4.9	1.6	hypotension			0.5	
Constipation			0.5	0.6	Myocardial infarction				0.3
flatulence	1.7		0.5	0.6	myocardialischemia			0.5	
Abdominal pain	1.7	5.1	3.9	4.2	pleurodynia				0.6
Diarrhea			1.9	1.3	Sensory system				
dyspepsia			1.9	2.9	tinnitus		1.7		
brash		1.7	4.4	2.9	rubefaction			0.5	0.3
anorexia		1.7		0.3	pruritus		1.7		
Appetite increased				0.3	ophthalic dryness			0.5	
gastricdysphoria	1.7		1.0	1.9	Musculoskeletal				
stomatitis				0.6	myalgia			1.0	0.6
glossitis	1.7			0.3	lumbago				0.3
thirst	3.4			0.3	back pain				0.3
stomatodysphoria	1.7		0.5	0.3	arthrosis				0.3
Nervous system					Urinary System				
Headache			2.9	1.3	oliguria				0.3
somnolence				0.3	Micturition frequency		1.7		
stupor				0.3	vaginitis				0.3
tension headache				0.3	Body as a whole				
Dizziness		3.4	1.9	0.6	edema	1.7	5.1	5.3	5.8
Respiratory					malaise			0.5	1.0
coughing				0.3	fever			0.5	0.3
dyspnea			0.5	0.3	algor			1.0	0.3
upper respiratory					pallor			0.5	
infection			1.5	1.9	wightgain			1.0	
epistaxis				0.3	wightloss				0.3
laryngoxerosis			0.5						

5. Precaution

1) Carefully consider the potential benefits and risks of pelubiprofen and other treatment options before deciding to use pelubiprofen. Use the lowest effective dose for the shortest duration consistent with individual patient treatment goals
2) Treatment with NSAIDs is an allopathic therapy for releaf.
3) Consider following precaution in use of pelubiprofen at Chronic disease
① Patients on long-term treatment with NSAIDs should have their CBC and chemistry profile checked periodically. If clinical signs and symptoms consistent with liver or renal disease develop, systemic manifestations occur (e.g., eosinophilia, rash etc.), or abnormal liver tests persist or worsen, pelubiprofen should be discontinued.
② Alternative therapies that do not involve NSAIDs should be considered.
4) Consider following precaution in use of pelubiprofen at Acute disease
① Acute inflammation, pain and fever should be monitored.
② Generally long-term treatment with same NSAIDs should be avoided.
③ Homeopathic therapy is recommended.
5) Monitoring of the patient's condition for evidence of adverse effect. Sever algro mortis, collapsing could occur. Infant with high fever(pyrexia), geriatric population or patients with wasting disease should be monitor carefully.
6) The pharmacological activity of pelubiprofen in reducing inflammation, and possibly fever, may diminish the utility of these diagnostic signs in detecting infectious complications of presumed noninfectious, painful conditions.
Patients with infection inflammation should be closely monitored carefully while on therapy with pelubiprofen.
7) Gastrointestinal (GI) Effects :
NSAIDs should be prescribed with extreme caution in patients with a prior history of ulcer disease or gastrointestinal bleeding. Patients with a prior history of peptic ulcer disease and/or gastrointestinal bleeding who use NSAIDs have a greater than 10-fold increased risk for developing a GI bleed compared to patients with neither of these risk factors. Other factors that increase the risk of GI bleeding in patients treated with NSAIDs include concomitant use of oral corticosteroids or anticoagulants, longer duration of NSAID therapy, smoking, use of alcohol, older age, and poor general health status. Most spontaneous reports of fatal GI events are in elderly or debilitated patients and therefore special care should be taken in treating this population.
8) Hypertension :
As with all NSAIDS, pelubiprofen can lead to the onset of new hypertension or worsening of pre-existing hypertension, either of which may contribute to the increased incidence of CV events. Patients taking thiazides or loop diuretics may have impaired response to these therapies when taking NSAIDs. NSAIDs, including pelubiprofen, should be used with caution in patients with hypertension. Blood pressure should be monitored closely during the initiation of therapy with pelubiprofen and throughout the course of therapy.
9) Congestive Heart Failure and Edema : Fluid retention and edema have been observed in some patients taking NSAIDs, including pelubiprofen.
Pelubiprofen should be used with caution in patients with fluid retention or heart failure.
10) Long-term administration of NSAIDs has resulted in renal papillary necrosis

and other renal injury. Renal toxicity has also been seen in patients in whom renal prostaglandins have a compensatory role in the maintenance of renal perfusion. In these patients, administration of an NSAID may cause a dose-dependent reduction in prostaglandin formation and, secondarily, in renal blood flow, which may precipitate overt renal decompensation.
Patients at greatest risk of this reaction are those with impaired renal function, heart failure, liver dysfunction, those taking diuretics and ACE inhibitors, angiotensin II receptor antagonists, and the elderly. Discontinuation of NSAID therapy is usually followed by recovery to the pretreatment state.

11) Advanced Renal Disease : No information is available from controlled clinical studies regarding the use of pelubiprofen in patients with advanced renal disease. Therefore, treatment with pelubiprofen is not recommended in these patients with advanced renal disease. If pelubiprofen therapy must be initiated, close monitoring of the patient's renal function is advisable.
12) Borderline elevations of one or more liver associated enzymes may occur in patients taking NSAIDs. These laboratory abnormalities may progress, may remain unchanged, or may be transient with continuing therapy. Rare cases of severe hepatic reactions, including jaundice and fatal fulminant hepatitis, liver necrosis and hepatic failure (some with fatal outcome) have been reported with NSAIDs, including pelubiprofen.
A patient with symptoms and/or signs suggesting liver dysfunction, or in whom an abnormal liver test has occurred, should be monitored carefully for evidence of the development of a more severe hepatic reaction while on therapy with pelubiprofen. If clinical signs and symptoms consistent with liver disease develop, or if systemic manifestations occur (e.g., eosinophilia, rash, etc.), pelubiprofen should be discontinued.
13) Anemia is sometimes seen in patients receiving NSAIDs, including pelubiprofen. Patients on long-term treatment with pelubiprofen should have their hemoglobin or hematocrit checked if they exhibit any signs or symptoms of anemia or blood loss.
NSAIDs inhibit platelet aggregation and have been shown to prolong bleeding time in some patients. Unlike aspirin, their effect on platelet function is quantitatively less, of shorter duration, and reversible. Patients receiving pelubiprofen tablets who may be adversely affected by alterations in platelet function, such as those with coagulation disorders or patients receiving anticoagulants should be carefully monitored.
14) Anaphylactoid Reactions : As with NSAIDs in general, anaphylactoid reactions have occurred in patients without known prior exposure to pelubiprofen.
This symptom complex typically occurs in asthmatic patients who experience rhinitis with or without nasal polyps, or who exhibit severe, potentially fatal bronchospasm after taking aspirin or other NSAIDs. Emergency help should be sought in cases where an anaphylactoid reaction occurs.
15) Skin Reactions : Pelubiprofen cause serious skin adverse events such as exfoliative dermatitis, Stevens Johnson syndrome (SJS), and toxic epidermal necrolysis (TENS), which can be fatal. These serious events can occur without warning and in patients without prior known allergy. Patients should be informed about the signs and symptoms of serious skin manifestations and use of the drug should be discontinued at the first appearance of skin rash or any other sign of hypersensitivity.
16) Patients with asthma may have aspirin-sensitive asthma. The use of aspirin in patients with aspirin-sensitive asthma has been associated with severe bronchospasm, which can be fatal. Since cross reactivity, including bronchospasm, between aspirin and other nonsteroidal anti-inflammatory drugs has been reported in such aspirin-sensitive patients, pelubiprofen should not be administered to patients with this form of aspirin sensitivity and should be used with caution in patients with preexisting asthma.
17) Pelubiprofen cannot be expected to substitute for corticosteroids or to treat corticosteroid insufficiency. Abrupt discontinuation of corticosteroids may lead to exacerbation of corticosteroid-responsive illness. Patients on prolonged corticosteroid therapy should have their therapy tapered slowly if a decision is made to discontinue corticosteroids.
18) Patients experience drowsiness, dizziness, vision impairment or other central nervous system disorder should avoid driving, machine work.

6. Drug Interactions

1) Avoid co-administration with other NSAIDs.
2) Pelubiprofen could increase the effect of other drugs. Co-administeration of drugs following should be done with caution. : sulfonylureas oral hypoglycemic agent(tolbutamide etc.), new quinolone antibiotics (enoxacin etc.).
3) ACE-inhibitors : Reports suggest that NSAIDs may diminish the antihypertensive effect of agniotensin comverting enzyme(ACE) inhibitors. This interaction should be given consideration in patients taking pelubiprofen concomitantly with ACE-inhibitors.
4) Aspirin : There is no consistent evidence that concurrent use of aspirin mitigates the increased risk of serious CV thrombotic events associated with NSAID use. The concurrent use of aspirin and an NSAID does increase the risk of serious GI events. Thus, concomitant administration of pelubiprofen and aspirin is not generally recommended because of the potential for increased serious GI event.
5) Furosemide and thiazide diuretics(Hydrochlorothiazide etc.) : Clinical studies have shown that NSAIDs can reduce the natriuretic effect of furosemide and thiazides in some patients.
This response has been attributed to inhibition of renal prostaglandin synthesis. During concomitant therapy with NSAIDs, the patient should be observed closely for signs of renal failure.
6) Lithium : NSAIDs produced an elevation of plasma lithium levels and a reduction in renal lithium clearance. This effect has been attributed to inhibition of renal prostaglandin synthesis by NSAIDs. Thus, when NSAIDs and lithium are administered concurrently, subjects should be observed carefully for signs of lithium toxicity.
7) Methotrexate : NSAIDs co-administrate with methotrexate could enhance the toxicity of methotrexate. Caution should be used when NSAIDs are administered concomitantly with methotrexate.
8) Coumarin-type anticoagulants (Wafarin etc.): The effects of warfarin and NSAIDs on GI bleeding could be synergistic, such that the users of both drugs together have a risk of serious GI bleeding higher than users of either drug alone. The physician should be cautious when administering pelubiprofen to patients with coumarin-type anticoagulants.

7. Pregnancy

1) In laboratory tests fetal toxicity(hight dose embryo/fetal death increase) has been reported. There are no studies in pregnant women, therefore, use of pelubiprofen during pregnancy should be avoided.
2) There are no adequate and well-controlled studies in pregnant women. In late pregnancy, as with other NSAIDs, pelubiprofen should be avoided because it may cause premature closure of the ductus arteriosus.
3) It has been reported that persistent fetal circulation(PFC) shown up in other NSAIDs.
4) In rat studies with NSAIDs, as with other drugs known to inhibit prostaglandin synthesis, an increased incidence of dystocia, delayed parturition, and decreased pup survival occurred.

8. Nursing mothers

Pelubiprofen is excreted in the milk of lactating rats, this drug should discontinue during nursing.

9. Pediatric Use

Safety has not been studied beyond pediatric patients.

10. Geriatric Use

To minimize the potential risk for an adverse event in geriatric patients, the lowest effective dose should be used for shortest duration possible, should be monitored carefully.

11. Storage

1) Keep out of the reach of children.
2) Store in original packaging for maintenance the quality and do not transfer the container as it could cause accident.

12. Others

1) Teratogenic effects: Carcinogenesis, mutagenesis, impairment of fertility
Pelubiprofen was not mutagenic in an Ames test and in vivo micronucleus test. Thus, chromosome aberration assay in mammalian cells appeared positive, more than 20% of chromosome aberration appeared at 60~350ßð/ml.
2) Impairment of fertility: reproductive
Animal reproductive test by rabbit embryo/fetal test parent gastrointestinal disorder appeared at 100mg/kg/day, fetation decreased at 300mg/kg/day. Rat perinatal mortality test shown increased in parent death at 3mg/kg/day, and decreased in live birth.

■ **STORAGE**
Light-resistant, well-closed container at room temperature

■ **PACKS** : 10, 100, 500 Tabs

■ **USE TERM** : 3 Years.

※ Medicine : Keep out of reach of children.

This drug is manufactured in accordance with Korea Good Manufacturing Practice(KGMP) as recommended by WHO.