Relaxmol-425™
Aceclofenac 100 mg and Paracetamol 325 mg Tablets

COMPOSITION
Each film coated tablet contains:
Aceclofenac IP 100 mg
Paracetamol IP 325 mg

PRODUCT DESCRIPTION
Relaxmol-425 is a fixed dose combination of Aceclofenac and Paracetamol. Aceclofenac belongs to a group of Non Steroidal Anti-inflammatory Drugs (NSAIDs) used to treat various painful inflammatory conditions. Aceclofenac has an outstanding anti-inflammatory profile mediated primarily through inhibition of cyclooxygenase (COX) activity and suppression of PGE2 synthesis. Paracetamol is a safe and effective analgesic-antipyretic agent with minimal effect on cardiovascular, respiratory and GI system. Paracetamol or acetaminophen is the deethyalted active metabolite of phenacetin. Chemically, Paracetamol is N-acetyl-p-aminophenol.

CLINICAL PHARMACOLOGY
Mechanism of Action:
Aceclofenac relieves pain and inflammation through a variety of mechanisms and in addition exerts stimulatory effects on cartilage matrix synthesis.

Anti-inflammatory Activity:
The anti-inflammatory effects of Aceclofenac have been shown in both acute and chronic inflammation. It inhibits various mediators of pain and inflammation including:
1. PGE2 via cyclooxygenase inhibition (COX-1 & COX-2) after intracellular metabolism to 4'hydroxy-aceclofenac and diclofenac in human rheumatoid synovial cells and other inflammatory cells.
2. IL-1β, IL-6 and tumor necrosis factor in human osteoarthritic synovial cells and human articular chondrocytes.
3. Reactive oxygen species (which play a role in joint damage) has also been observed in patients with osteoarthritis of knee.
4. Expression of cell adhesion molecules (which is implicated in cell migration and inflammation) has also been shown in human neutrophils.

Stimulatory effects on cartilage matrix synthesis:
Aceclofenac stimulates glycosaminoglycan synthesis in human osteoarthritic cartilage by inhibition of IL-1β and suppresses cartilage degeneration by inhibiting IL-1β mediated promatrix metalloproteinase production and proteoglycan release.
Paracetamol is a clinically proven analgesic and antipyretic agent with weak anti-inflammatory effect.

Analgescic Action:
The central analgesic action of Paracetamol resembles that of aspirin. It produces analgesia by raising pain threshold.

Antipyretic effect:
The antipyretic effect of Paracetamol is attributed to its ability to inhibit COX in the brain where peroxide tone is low.
Recent evidence suggests inhibition of COX-3 (believed to be splice variant product of the COX-1 gene) could represent a primary central mechanism by which Paracetamol decreases pain and possibly fever.

PHARMACOKINETICS
Aceclofenac is well absorbed from gastrointestinal tract and peak plasma concentrations (Cmax) are reached 1-3 hours after an oral dose. The drug is more than 99% bound to plasma proteins and the volume of distribution (Vd) is approximately 25 liters. The presence of food reduced rate of absorption (increased tmax) but not the extent of absorption (Cmax or AUC). In patients with knee pain and synovial fluid effusion, the plasma concentration of Aceclofenac was twice that in synovial fluid after multiple doses of the drug.
Aceclofenac is metabolized mainly to 4'-hydroxy-aceclofenac. The drug is eliminated primarily through renal excretion with 70-80% of administered dose found in urine as glucuronides and rest being excreted in faeces. The plasma elimination half life of Aceclofenac is approximately 4 hours.
Paracetamol is rapidly and almost completely absorbed from gastrointestinal tract with peak plasma concentrations (Cmax) occurring about 10 to 60 minutes after oral administration. Plasma protein binding is negligible at usual therapeutic concentration but increases with increasing concentrations. Acetaminophen is relatively uniformly distributed throughout most body fluids. The plasma half life (t1/2) 2-3 hours and the effect after oral dose lasts for 3-5 hours. Paracetamol is metabolized predominantly in liver and excreted in the urine mainly as glucuronide and sulfate conjugate. Less than 5% is excreted unchanged.

**SPECIAL POPULATIONS**

As with other NSAIDs and combinations, caution is advised in elderly patients who are more likely to have concomitant renal, hepatic or cardiovascular impairment or receiving concurrent medication. In patients with hepatic impairment, dosage reductions are recommended. RELAXMOL-425 should be avoided in patients with moderate and severe renal impairment. Regular use of RELAXMOL-425 during pregnancy and lactation should be avoided, unless the potential benefits outweigh the risks.

**THERAPEUTIC INDICATIONS**

RELAXMOL-425 is indicated for relief from severe pain and inflammation in Osteoarthritis, Rheumatoid arthritis, Ankylosing spondylitis, Low back pain, Dental pain, Gynaecological pain and painful & Inflammatory conditions of ear, nose & throat.

**DOSAGE**

The recommended dose of RELAXMOL-425 is 1 tablet twice daily. Generally, no dose adjustment is necessary in elderly patients and those with mild renal impairment. Safety and efficacy has not been established in children. Keep out of reach of children.

**CAUTION**

Overdose of this drug has potential of severe liver injury and allergic reactions. (Example - swelling of face, mouth and throat, difficulty in breathing, itches or rashes)

**ADVERSE REACTION**

Most of the adverse events are minor and reversible with treatment discontinuation. The majority of side effects are related to gastrointestinal system (dyspepsia, abdominal pain, nausea and diarrheaa), most frequent being dyspepsia, abdominal pain and rise in hepatic enzymes. Other rare side-effects include dizziness, constipation, vomiting, ulcerative stomatitis, rash, dermatitis, headache, fatigue, allergic reactions, anemia, granulocytopenia, thrombocytopenia, neutropenia, oedema, palpitation, leg cramps, flushing, purpura, paraesthesia, tremors, gastrointestinal bleeding, gastrointestinal ulceration, pancreatitis, interstitial nephritis, depression, abnormal dreaming, somnolence, insomnia, vasculitis, hypoglycemia, rise in blood urea, serum creatinine and serum potassium. As with other NSAIDs, severe mucocutaneous skin reactions may occur.

**CONTRAINdications**

RELAXMOL-425 is contraindicated in the following situations:
- Patients sensitive to Acelofenac, Paracetamol or to any of the excipients of the product
- Patients in whom aspirin or other NSAIDs, precipitate attacks of bronchospasm, Acute rhinitis or urticaria or patients hypersensitive to these drugs.
- Patients with active or suspected peptic ulcer or gastrointestinal bleeding or bleeding disorders.
- Patients with severe heart failure, hypertension, hepatic or renal insufficiency
- Third trimester of pregnancy

**PRECAUTIONS**

RELAXMOL-425 may cause dizziness. Driving or operating machinery is to be avoided. Individuals receiving long-term treatment should be regularly monitored for renal function tests, liver function tests and blood counts. It is to be used with caution in hepatic porphyria, coagulation disorders, history of peptic ulcers, ulcerative colitis, Crohn's disease, SLE, cerebrovascular bleeding, pregnancy and lactation. Caution should be exercised in patients with mild to moderate impairment of cardiac, hepatic or renal function and in elderly patients who are more likely to be suffering from these conditions. Caution is also required in patients on diuretic therapy or otherwise at risk of hypovolemia.

**DRUG INTERACTION**

Drug interactions associated with Acelofenac are similar to those observed with other NSAIDs. Acelofenac may increase the plasma concentrations of lithium, digoxin and methotrexate. It may increase the activity of anticoagulants, Inhibit the activity of diuretics, enhance cyclosporine nephrotoxicity and precipitate convulsions when coadministered with quinolone antibiotics. Coadministration of Acelofenac with other NSAIDs and corticosteroids are to be avoided due to increased incidence of side-effects. The risk of Paracetamol toxicity may be increased in patients receiving other potentially hepatotoxic drugs or drugs that induce hepaticmicrosomal enzymes. Coadministration of Paracetamol with rifampicin, isoniazid, chloramphenicol, anti-epileptic drugs and antiviral drugs is to be avoided. Metoclopramide may increase the absorption of Paracetamol whereas excretion and plasma concentration may be altered when coadministered with probenecid. Cholestyramine also reduces the absorption of Paracetamol.

**OVERDOSAGE**

Overdose may cause nausea, vomiting, pain abdomen, dizziness, somnolence, headache, sweating, pancreatitis, hepatic failure and acute renal failure. Treatment, if required, includes gastric lavage, activated charcoal and other symptomatic measures as per medical advice.

**STORAGE INSTRUCTIONS**

Store below 25°C away from direct sunlight.

**PRESENTATION AND PACKING**

10 Tablets in Blister Pack.

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