

**ACEPAR-MR CAPLETS**  
**Aceclofenac, Paracetamol and Chlorzoxazone Tablets**

**Composition:**

Each film coated caplet contains:	
Aceclofenac BP	100mg.
Paracetamol BP	500mg.
Chlorzoxazone USP	375mg.

**Pharmacology:**

**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:

- PGE<sub>2</sub> 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.

- IL-1 $\beta$ , IL-6 and Tumor necrosis factor in human osteoarthritic synovial cells and human articular chondrocytes.

- Reactive oxygen species (which plays a role in joint damage) has also been observed in patients with osteoarthritis of knee.

- 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-1 $\beta$  and suppresses cartilage degeneration by inhibiting IL-1 $\beta$  mediated pro-matrix metalloproteinase production and proteoglycan release.

**Paracetamol** is a clinically proven analgesic and antipyretic agent with weak anti-inflammatory effect.

**Analgesic action:** 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.

**Chlorzoxazone** is a centrally acting skeletal muscle relaxant with sedative properties. It is claimed to inhibit muscle spasm by exerting an effect primarily at the level of the spinal cord and subcortical areas of the brain. Its effects begin within an hour of an oral dose and last for 3 to 4 hours.

**Pharmacokinetics:**

**Aceclofenac** is well absorbed from gastrointestinal tract and peak plasma concentrations (C<sub>max</sub>) are reached 1-3 hours after an oral dose.

The drug is more than 99% bound to plasma proteins and the volume of distribution (V<sub>d</sub>) is approximately 25 litres. The presence of food reduced rate of absorption (increased t<sub>max</sub>) but not the extent of absorption (C<sub>max</sub> 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 (C<sub>max</sub>) occurring about 10 to 60 minutes after oral administration. Plasma protein binding is negligible at usual therapeutic concentration but increases with increasing concentrations. Paracetamol is relatively uniformly distributed throughout most body fluids. The plasma half life (t<sub>1/2</sub>) 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.

**Chlorzoxazone** is reported to be completely absorbed after oral doses and peak plasma concentrations are achieved after 1 to 2 hours.

It is rapidly metabolised in the liver via the cytochrome P450 isoenzyme CYP2E1, mainly to 6-hydroxychlorzoxazone, and excreted in the urine primarily as the glucuronide metabolite. The elimination half-life of chlorzoxazone is about 1 hour.

**Indications:**

ACEPAR - MR caplets is indicated for relief of 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. It is also used in the symptomatic treatment of painful muscle spasm associated with musculoskeletal conditions.

**Dosage & Administration:**

The usual dose of ACEPAR MR is 1 tablet twice daily by mouth. One tablet in the morning and one in the evening. There is some evidence that the dose of ACEPAR MR should be reduced in patients with hepatic impairment and it is suggested that an initial daily dose of 1 tablet to be taken.

**Contraindications:**

Hypersensitivity, gastrointestinal bleeding, moderate to severe renal impairment and pregnancy.

**Side Effects:**

Nausea, allergic reactions, skin rashes, acute renal tubular necrosis, diarrhoea, headache, vertigo, dizziness, nervousness, tinnitus, depression, drowsiness, insomnia, fever, angioedema, bronchospasm, rashes and blood dyscrasias.

**Drug Interactions:**

Aceclofenac may increase the plasma concentrations of lithium & digoxin. Concomitant use of aceclofenac & diuretics may inhibit the activity of diuretics. The activity of anticoagulants may be enhanced when used concomitantly with aceclofenac. Additive CNS depression may occur when chlorzoxazone is administered concomitantly with other CNS depressants, including alcohol. Absorption of paracetamol may be reduced by pethidine & propranolol.

**Pregnancy and lactation:**

Aceclofenac and chlorzoxazone are contraindicated during pregnancy and breastfeeding hence the combination cannot be used.

**Overdosage:**

Management of acute poisoning with NSAIDs essentially consists of supportive and symptomatic measures.

**Presentation:**

Bulk packs of 30 caplets in HDPE containers.

B blister pack of 1 x 10's per unit box.

**Storage conditions:**

Store below 30°C. Protect from direct sunlight.

Keep all medicines out of reach of children.

**Manufactured By:**



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