NOTOPAIN® CAPLETS

Diclofenac Sodium + Paracetamol

Composition

Each tablet contains: Diclofenac Sodium BP 50mg Paracetamol BP 500mg

Pharmacology

Phamacodynamics

Diclofenac 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 Diclofenac have been shown in both acute and chronic inflammation. It inhibits various mediators of pain and inflammation including:

- 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.
- IL-IB, 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: Diclofenac stimulates glycosaminoglycan synthesis in human osteoarthritis cartilage by inhibition of IL-1B and suppresses cartilage degeneration by inhibiting IL-IB mediated pro-matrix metalloproteinase production and proteoglycan release.

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

Analgesic action: The central analgesic action of paracetamol resembles that of aspirin. It produces analgesia by raising pain threshold.

Antipyretic effects: The antipyretic effect of paracetamol is attributed as its ability to inhibit COX in the brain where peroxide tone is low.

Recent evidence suggests inhibition of COX-3 (believed to be splice varient product of the COX-1 gene) could represent primary central mechanism by which paracetamol decreases pain and possibly fever.

Pharmacokinetics

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 increase concentrations.

Paracetamol 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 sulphate conjugate. Less than 5% is excreted unchanged.

Diclofenac is 100% absorbed after oral administration compared to IV administration as measured by urine recovery. However, due to first-pass metabolism, only about 50% of the absorbed dose is systematically available. In some fasting normal volunteers, measurable plasma levels are observed within 10 minutes of dosing with Diclofenac. Peak plasma levels are achieved approximately 1hours in fasting normal volunteers, with a range of 33 minutes to 2hours. Food has no significant effect on the extent of diclofenac absorption and a reduction in peak plasma levels of approximately 30%.

Mechanism of Action

Diclofenac sodium caplets are a non-inflammatory drug (NSAID) that exhibits anti-inflammatory, analgesic and antipyretic activities in animal models. The mechanism of action of diclofenac sodium caplets, like that of other NSAIDs is not completely understood but may be related to prostaglandin synthetase inhibition. Paracetamol has analgesic and antipyretic actions. Rationale of Combination of Diclofenac Sodium & Paracetamol Diclofenac is a time tested prompt acting analgesic with anti-inflammatory actions, Paracetamol is a time tested antipyretic with analgesic & anti-inflammatory actions. This medicine contains time tested analgesic, antioyretic with both having anti-inflammatory actions too.

Indications

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

Dosage and Administration

The maximum recommended dose of NOTOPAIN is two caplets daily, as one caplet in the morning and one in the evening.

Contraindications

- Patients sensitive to 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

Warning and precautions

This medicine may cause dizziness. Driving or operating machinery are to be avoided. Individual receiving long-term treatments 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, Cohn'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 likely to be suffering from these conditions. Caution is also required in patients on diuretic therapy or otherwise at risk of hypovolemia.

Drug Interactions

Drug interactions associated with Paracetamol are similar to those observed with other NSAIDs. Paracetamol may increase the plasma

concentrations in lithium, digoxin and methotrexate. It may increase the activity of anticoagulants, inhibits the activity of diuretics, enhances, cyclosporine nehrotoxicity and precipitate convulsions when co administered with quinolone antibiotics, Co administration of Paracetamol 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 potentiality heatotoxic drugs or drugs that induce hepatic microsomal enzymes.

Cpadministration of Paracetamol with rifampicin, Isoniazid, Chlorarnphenicol, antiepileptic drugs and antiviral drugs is to be avoided. Metoclopromide may increase the absorption of Paracetamol whereas excretion and plasma concentration may be altered when co administered with probenecid. Choiestyramine also reduces the absorption of Paracetamol.

Over dosage

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

Storage

Store in an airtight container, protect from light

Presentation: 10 caplets in Blister pack

Keep medicine out of reach of children