COMPOSITION :

Each film coated tablet contains:

Aceclofenac BP	……..	100 mg
Paracetamol IP	……..	325 mg
Serratiopeptidase	……..	15 mg

Colour: Titanium oxide and red oxide of iron.

Vexipar™-AC Plus

PHARMACOLOGY :

PHARMACODYNAMICS:

Aceclofenac: Aceclofenac is an NSAID known to exhibit multifactor mechanism of action. Aceclofenac was developed in order to provide a highly effective pain relieving therapy with a reduced side effect profile.

1. Aceclofenac directly blocks PGE 2 secretion at the site of inflammation by inhibiting IL-Beta & TNF in the inflammatory cells (Intracellular Action).Aceclofenac has been demonstrated to inhibit cyclooxygenase (COX) activity and to suppress the PGE 2 production by inflammatory cells, which are likely to be a primary source of PGE 2 . Inflammatory cells release IL-1 and TNF, which produce PGE 2 by induction of COX-2. Aceclofenac and 4`-hydroxyaceclofenac penetrate the inflammatory cells like polymorphonuclears, monocytes and rheumatoid synovial cells and get hydrolyzed to the active metabolites diclofenac and 4`-hydroxydiclofenac which inhibit IL-1 and TNF released by the inflammatory cells and therefore suppress production of PGE 2 at the site of inflammation.

2. Aceclofenac stimulates the synthesis of the extracellular matrix of the Human Articular Cartilages. Aceclofenac blocks degeneration and stimulates synthesis of extracellular matrix of cartilages by inhibiting the action of different cytokines. Aceclofenac and the metabolites inhibit IL-6 production by human chondrocytes. This leads to inhibition of increase of inflammatory cells in synovial tissue, inhibition of IL-1 amplification, inhibition of increased MMP synthesis and thus ensuring proteoglycan production. Aceclofenac also inhibits IL-1 and TNF production by human chondrocytes, inflammatory cells and synovial cells and therefore blocks suppression of GAG and collagen synthesis and stimulates growth factor mediated synthesis of GAG and collagen. 4`-hydroxyaceclofenac, a metabolite of aceclofenac inhibits pro MMP1 and pro MMP3 produced by synovial cells (Rheumatoid Synovial Cells) in serum and in synovial fluid and thus inhibits progressive joint destruction by MMPs.

3. Aceclofenac inhibits Neutrophil Adhesion & Accumulation at the inflammatory site in the early phase and thus blocks the pro-inflammatory actions of Neutrophils.

Paracetamol:

Paracetamol is a peripherally acting analgesic and is well absorbed orally. Paracetamol produces analgesia by elevation of the pain threshold and antipyresis through action on the hypothalamic heat-regulating center. Paracetamol is equal to aspirin in analgesic and antipyretic effectiveness.

Serratiopeptidase:

It binds to alpha-2-macroglobulin in the blood in the ratio of 1:1, which helps to mask its antigenicity but retain its enzymatic activity. Levels of serratiopeptidase are slowly transferred to the exudate at the site of inflammation and gradually the blood level decline.

By hydrolysing bradykinin, histamine and serotonin, it indirectly reduces dilatation of blood capillaries and controls permeability. Serratiopeptidase blocks plasmin inhibitors thus helping the fibrinolytic activity of plasmin. Degradation of ` extra-fibrin` to small fragment prevents clogging of microcapillaries, helps clearance of exudates, reduces swelling and improves microcirculation.

Serratiopeptidase:

Aceclofenac:

Absorption: After oral administration, aceclofenac is rapidly absorbed and the bioavailability is almost 100%. Peak plasma concentrations are reached approximately 1.25 to 3 hours following ingestion. T max is delayed with concomitant food intake whereas the degree of absorption is not influenced.

Distribution: Aceclofenac is highly protein-bound (> 99.7%). Aceclofenac penetrates into the synovial fluid where the concentrations reach approximately 60% of those in plasma. The volume of distribution is approximately 30L.

Metabolism: Aceclofenac is probably metabolized via CYP2C9 to the main metabolite 4-hydroxyaceclofenac. The mean plasma elimination half-life is 4-4.3 hours.

Excretion:

Approximately two-thirds of the administered dose is excreted via the urine, mainly as conjugated hydroxymetabolites. Only 1% of an oral single dose is excreted unchanged. A slower rate of elimination of aceclofenac has been detected in patients with decreased liver function after a single dose of aceclofenac. In a multiple dose study using 100 mg once daily, there was no difference in the pharmacokinetic parameters between subjects with mild to moderate liver cirrhosis and normal subjects. In patients with mild to moderate renal impairment, no clinically significant differences in the pharmacokinetics were observed after a single dose.

Paracetamol:

The plasma elimination half-life ranges from 1 to 4 hours for paracetamol. Paracetamol is distributed throughout most fluids of the body, and is metabolized primarily in the liver. Little unchanged drugs is excreted in the urine, but most metabolic products appear in the urine within 24 hours.

Serratiopeptidase:

On oral administration, serratiopeptidase is absorbed in GI tract and distributed throughout the body tissues unchanged via systemic circulation. It reaches in higher concentration in inflamed tissues. A considerable amount of drug is in the lymph and blood. The concentration in the lymph was found two times higher than in blood. Serratiopeptidase levels in inflammatory exudates rises gradually with decline in blood levels indicating that serratiopeptidase is quite rapidly transferred to the site of inflammation.

INDICATIONS:

- Oedema and swelling
- Joint pains and trauma
- Dental pain
- Post operative pain
- Pelvic inflammatory disease
- Deep Epiosiotomy
- Caesearian cases

DOSAGE AND ADMINISTRATION:

Two tablets in a day.

CONTRAINDICATIONS:

VEXIPAR-AC PLUS should not be administered to patients hypersensitive to aceclofenac or paracetamol other NSAIDs, or patients with a history of aspirin or NSAID related allergic or anaphylactic reactions or with peptic ulcers or GI bleeding, moderate or severe renal impairment.

DRUG INTERACTIONS:

Drug interactions associated with aceclofenac are similar to those observed with other NSAIDs. Aceclofenac may increase plasma concentrations of lithium, digoxin and methotrexate, increase the activity of anticoagulants, inhibit the activity of diuretics, enhance cyclosporin nephrotoxicity and precipitate convulsions when co-administered with quinolone antibiotics. When concomitant administration with potassium sparing diuretics is employed, serum potassium should be monitored. Furthermore, hypo or hyperglycaemia may result from the concomitant administration of aceclofenac and antidiabetic drugs, although this is rare. The co-administration of aceclofenac with other NSAIDs or corticosteroids may result in increased frequency of side effects. Caution should be exercised if NSAIDs and methotrexate are administered within 2-4 hours of each other, since NSAIDs may increase methotrexate plasma levels, resulting in increased toxicity.

ADVERSE EFFECTS:

The majority of adverse reactions reported have been reversible and of a minor nature. The most frequent are gastro-intestinal disorders, in particular dyspepsia, abdominal pain, nausea and diarrhea, and occasional occurrence of dizziness. Dermatological complaints including pruritus and rash and abnormal hepatic enzyme and serum creatinine levels have also been reported.

Undesirable effects associated with NSAIDs in general:
Gastrointestinal: The most commonly observed adverse events are gastrointestinal in nature. Peptic ulcers, perforation or GI bleeding, sometimes fatal, particularly in the elderly, may occur. Nausea, vomiting, diarrhea, flatulence, constipation, dyspepsia, abdominal pain, melaena, haematemesis, ulcerative stomatitis, exacerbation of colitis and Crohn`s disease have been reported following administration. Less frequently, gastritis has been observed. \Vascular and cardiac disorders: Oedema, hypertension and cardiac failure have been reported in association with NSAID treatment .Clinical trial and epidemiological data suggest that use of some NSAIDs (particularly at high doses and in long term treatment) may be associated with an increased risk of arterial thrombotic events (for example myocardial infarction or stroke).

Other rare or very rare class effects reported with NSAIDs in general are:
Blood and the lymphatic system disorders – Aplastic anaemia
Psychiatric disorders – Hallucination, Confusional state
Nervous system disorders – Optic neuritis, somnolence
Ear and labyrinth disorders – Tinnitus
Respiratory, thoracic and mediastinal disorders – Aggravated asthma
Skin and subcutaneous tissue disorder – Toxic epidermal necrolysis, Erythema multiforme, Exfoliative dermatitis, photosensitivity reaction. Renal and urinary disorders – Interstitial nephritis
General disorders and administration site conditions – Malaise.

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OVERDOSAGE:

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

PACKAGING INFORMATION:

VEXIPAR-AC PLUS is available in a strip of 10 tablets.