PRESCRIBING INFORMATION: For the use of Registered Medical Practitioner or a Hospital or a Laboratory only.

HIFENAC-P

Aceclofenac & Paracetamol Tablets (100 + 500) mg

COMPOSITION:
Each uncoated tablet contains:

Aceclofenac BP	100 mg
Paracetamol BP	500 mg

DESCRIPTION
Aceclofenac is a non-steroidal agent with marked anti-inflammatory and analgesic properties. The chemical name of aceclofenac is 2-[2-[2(2, 6-dichlorophenyl) aminophenyl] acetyl] oxyacetic acid.

Paracetamol is a 4'-hydroxyacetanilide, is a non-opiate, non-salicylate analgesic and antipyretic. The chemical name for paracetamol is N-acetyl-p-aminophenol

HIFENAC-P is a combination of aceclofenac and paracetamol has been specially formulated to provide the relief to patients suffering from pain, inflammation and fever.

CLINICAL PHARMACOLOGY

***Mechanism of action*:**

Aceclofenac: The mode of action of aceclofenac is largely based on the inhibition of prostaglandin synthesis. Aceclofenac is a potent inhibitor of the enzyme cyclo-oxygenase, which is involved in the production of prostaglandins.

Paracetamol: Paracetamol is a peripherally acting analgesic and is well absorbed orally. Paracetamol produces analgesia by elevation of the pain threshold and antipyretic action through action on the hypothalamic heat regulating center

***Pharmacokinetics*:**

Aceclofenac: After oral administration, aceclofenac is rapidly and completely absorbed as unchanged drug. Peak plasma concentrations are reached approximately 1.25 to 3.00 hours following ingestion. Aceclofenac penetrates into the synovial fluid, where the concentrations reach approximately 57% of those in plasma. The volume of distribution is approximately 25 L.

The mean plasma elimination half-life is around 4 hours. Aceclofenac is highly protein-bound (>99%). Aceclofenac circulates mainly as unchanged drug. 4'-hydroxyaceclofenac is the main metabolite detected in plasma. Approximately two-thirds of the administered dose is excreted via the urine, mainly as hydroxymetabolites.

Paracetamol: The plasma elimination half-life ranges from 1 to 4. Paracetamol is distributed throughout most fluids of the body, and is metabolized primarily in the liver. Little unchanged drug is excreted in the urine, but most metabolic products appear in the urine within 24 hours. Paracetamol appears to be widely distributed throughout most body tissues except fat. Its apparent volume of distribution is about 0.9 L/kg. A relative small portion (~20%) of paracetamol is bound to plasma protein. Paracetamol is primarily metabolized in the liver and involves three principal separate pathways: a) conjugation with glucuronide; b) conjugation with sulfate; and c) oxidation via the cytochrome, P450-dependent, mixed-function oxidase enzyme pathway to form a reactive intermediate metabolite, which conjugates with glutathione and is then further metabolized to form cysteine and mercapturic acid conjugates. The principal cytochrome P450 isoenzyme involved appears to be CYP2E1, with CYP1A2 and CYP3A4 as additional pathways.

INDICATIONS
HIFENAC-P is indicated for the treatment of acute painful inflammatory conditions with or without associated fever.

DOSAGE
One tablet twice daily, the maximum recommended dose of HIFENAC-P is two tablets daily,

CONTRAINDICATIONS
- Hypersensitivity to Aceclofenac or Paracetamol or any component of the tablet.
- In patients in whom substances with a similar action (e.g. other NSAIDs), precipitate attacks of asthma, bronchospasm, acute rhinitis or urticaria or patients are hypersensitive to these drugs.
- Severe heart failure or severely impaired hepatic or renal organ function and during the last three months of pregnancy.

WARNINGS AND PRECAUTIONS
Close medical surveillance is imperative in patients with symptoms indicative of gastrointestinal disorders, with a history suggestive of gastrointestinal ulceration, with ulcerative colitis or with Crohn`s disease, bleeding diathesis or haematological abnormalities.
Where gastrointestinal bleeding or ulceration occurs in patients receiving aceclofenac, the drug should be withdrawn. Close medical surveillance is also imperative in patients suffering from severe impairment of hepatic function.
Aceclofenac should be given with caution to elderly patients with renal, hepatic or cardiovascular impairment and to those receiving other medication. The lowest effective dose should be used and renal function monitored regularly.
As with other NSAIDs, allergic reactions, including anaphylactic/ anaphylactoid reactions, can also occur without earlier exposure to the drug.

	Checked by				Approved by
Department	PMQC	RA	Packing Dev.	Q.A.	Head Q.A.
Signature					
Date					

Product Name : HIFENAC-P
Size : 140 x 210 (mm)
Folding Size : 140 x 30 (mm)
No. of Col. : 1
Date : 27/09/15

File name : 8609882-HIFENAC-P-PIL
Col. Shade No. : Pantone Black

The importance of prostaglandins in maintaining renal blood flow should be taken into account in patients with impaired cardiac or renal function, those being treated with diuretics or recovering from major surgery. Effects on renal function are usually reversible on withdrawal of aceclofenac.
Caution should also be exercised in patients with history of coagulation defects and history of liver dysfunction.
Renal and hepatic function and blood counts should be monitored during long term treatment. Persistently elevated hepatic enzyme levels necessitate withdrawal of aceclofenac.
Chronic heavy alcohol abusers may be at increased risk of liver toxicity from excessive paracetamol use.
Renal impairment: Patients with mild renal impairment should be kept under surveillance since the use of NSAIDs may result in deterioration of renal function. The lowest effective dose should be used and renal function monitored regularly.
Hepatic impairment: The recommended initial dose of HIFENAC-P should be reduced to one tablet daily in patients with impaired hepatic function.
Pregnancy & lactation: The drug in not recommended in pregnant & breast-feeding women.
Paediatric use: There are no clinical data available on the use of aceclofenac in children.
Geriatric use: Generally no dose reduction is necessary, however, consider the precautions.

DRUG INTERACTIONS
Drug interactions associated with **HIFENAC-P** 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 hyperglycemia 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.
Potential hepatotoxicity of Paracetamol may be increased by large doses or long-term administration of barbiturates, carbamazepine, hydantoins, isoniazid, rifampin and sulfinpyrazone.

ADVERSE EFFECTS

***Commonly reported adverse reactions*:**
Aceclofenac:
The majority of side effects observed have been reversible and of a minor nature and include gastro-intestinal disorders (dyspepsia, abdominal pain, nausea and diarrhea) and occasional occurrence of dizziness. Dermatological complaints including pruritus and rash and abnormal hepatic enzyme levels and raised serum creatinine have occasionally been reported.

Paracetamol:
Side effects are usually mild and may include gastro-intestinal disorders, skin rashes and other allergic reactions occasionally.

OVERDOSAGE
Aceclofenac:
Management of acute poisoning with NSAIDs essentially consists of supportive and symptomatic measures. There are no human data available on the consequences of aceclofenac overdosage. The therapeutic measures to be taken are: absorption should be prevented as soon as possible after overdosage by means of gastric lavage and treatment with activated charcoal; supportive and symptomatic treatment should be given for complications such as hypotension, renal failure, convulsions, gastro-intestinal irritation, and respiratory depression; specific therapies such as forced diuresis, dialysis or haemoperfusion are probably of no help in eliminating NSAIDs due to their higher protein binding and extensive metabolism.

Paracetamol:
Serious potential consequences of paracetamol overdosage are hepatic centrilobular necrosis, leading to hepatic failure and death, renal tubular necrosis, hypoglycemia and coagulation defects. Early symptoms following a potentially hepatotoxic overdose may include: nausea, vomiting, diaphoresis and general malaise. Clinical and laboratory evidence of hepatic toxicity may not be apparent until 48 to 72 hours post ingestion. In cases of overdose, the stomach should be emptied promptly by lavage or by induction of emesis. Standard recommendations should be followed for the treatment of paracetamol overdose.

STORAGE
Store below 30° C, protected from light.

PRESENTATION
HIFENAC-P is available in a blister of 10 tablets.

Manufactured by:
INTAS
INTAS PHARMACEUTICALS LTD.
Selaqui, Dehradun-248 197. INDIA

80 857 0 8609882

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