1.3 PRODUCT INFORMATION

1.3.1 Summary of Product Characteristics

1.3.2 Labelling

1.3.3 Package Insert

Enclosed.

1.3.1 SUMMARY OF PRODUCT CHARACTERISTICS

Enclosed

1.3.1. SUMMARY OF PRODUCT CHARACTERICTICS

1. NAME OF THE MEDICINAL PRODUCT:

1.1 Product name:Zerodol-P (Aceclofenac and Paracetamol Tablets)

1.2 Strength: Aceclofenac BP ..... 100 mg
Paracetamol BP .....500 mg

1.3 Pharmaceutical dosage form: Tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION:

2.2 Quantitative Declaration:
Each film coated tablets contains
Aceclofenac BP ..... 100 mg
Paracetamol BP .....500 mg

3. PHARMACEUTICAL FORM:

Yellow coloured oval shaped film coated tablets, plain on both the side

4. CLINICAL PARTICULARS:

4.1 INDICATIONS

Rheumatoid arthritis, osteoarthritis, ankylosing spondylitis, cervical spondylitis, intervertebral disc syndrome, sciatica, non-articular rheumatic conditions, post-operative and traumatic inflammations, painful inflammatory conditions in gynaecology and dentistry and pain and fever associated with inflammation

4.2. Posology and Method of Administration

The recommended dose of UPRIGHT 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.

4.3. Contra-indications

The combination should not be administered to:
•Patients sensitive to Aceclofenac, 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

4.4 Special Warnings and Special Precautions for Use

Warnings
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.

Gastrointestinal bleeding or ulcerative perforation, haematemesis and melaena have in general more serious consequences in the elderly. They can occur at any time during treatment, with or without warning symptoms or previous history. In the rare instances, 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.

As with other NSAIDs, allergic reactions, including anaphylactic/anaphylactoid reactions, can also occur without earlier exposure to the drug.

Precautions
It may cause dizziness. Driving or operating machinery are 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 interactions
Drug interactions associated with Aceclofenac are similar to those observed with other NSAIDs. Aceclofenac may increase the plasma concentrations of lithium, digoxin and methotrexate. It may increase

the activity of anticoagulants, inhibit the activity of diuretics, enhance cyclosporine nehrotoxicity and precipitate convulsions when coadministered with quinolone antibiotics. Coadministration of Aceclofenac 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 heatotoxic drugs or drugs that induce hepatic microsomal enzymes. Coadministration of Paracetamol with rifampicin, isoniazid, chloramphenicol, anti-epileptic drugs and antiviral drugs is to be avoided. Metoclopromide 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.

4.5. Interaction with other Medicinal Products and other forms of Interaction

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 coadministered 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 coadministration of aceclofenac with other NSAIDs or corticosteroids may result in increased frequency of adverse events.

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.

4.6. Pregnancy and Lactation

The safety of this medicine for use during pregnancy has not been established. The drug is not recommended in pregnant or breast feeding women.

4.7. Effects on Ability to Drive and Use Machines

Patients who experience dizziness or other central nervous system disturbances while taking NSAIDs should refrain from driving or operating machinery.

4.8. Undesirable Effects

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 diarrhea), 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.

The following adverse events (described as most frequent >5%, occasional < 5% or rare cases < 0.1%) were reported during all clinical trials:

Gastrointestinal disorders: Most frequent: dyspepsia (7.5%), abdominal pain (6.2%), Occasional: nausea (1.5%), diarrhoea (1.5%), flatulence (0.8%), gastritis (0.6%), constipation (0.5%), vomiting (0.5%), ulcerative stomatitis (0.1%). Rare cases: (all <0.1%) pancreatitis, melaena, stomatitis

Central and peripheral nervous system: Occasional: dizziness (1%), vertigo (0.3%). Rare cases: (all <0.1%), paraesthesia, tremor

Psychiatric: Rare cases: (all <0.1%) depression, abnormal dreaming, somnolence, insomnia

Skin and appendages: Occasional: pruritus (0.9%), rash (0.5%), dermatitis (0.2%). Rare cases: (all <0.1%) eczema

Liver and biliary: Occasional: hepatic enzymes increased (2.5%)

Metabolic: Occasional: BUN increased (0.4%), blood creatinine increased (0.3%). Rare cases (all <0.1%) alkaline phosphatase increased, hyperkalaemia

Cardiovascular: Rare cases: (all <0.1%) oedema (dependent), palpitation, leg cramps, flushing, purpura

Respiratory: Rare cases: (all <0.1%) dyspnoea, stridor

Blood: Rare cases: (all <0.1%) anaemia, granulocytopenia, thrombocytopenia

Body as whole, general: Rare cases: (all <0.1%) headache, fatigue, face, oedema, hot flushes, allergic reaction, weight increase

Other: Rare cases: (all < 0.1%) abnormal vision, abnormal taste

4.9. Overdose

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, gastrointestinal irritation, and respiratory depression, specific therapies such as forced diuresis, dialysis or haemoperfusion are probably of no help in eliminating NSAIDs due to their high rate of protein binding and extensive metabolism.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic Properties

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.

Aceclofenac has been shown to exert effects on a variety of mediators of inflammation. The drug inhibits synthesis of the inflammatory cytokines interleukin (IL)- and tumour necrosis factor and inhibits prostaglandin E2 (PGE2) production. Effects on cell adhesion molecules

from neutrophils have also been noted. In vitro data indicate inhibition of cyclo-oxygenase (COX)-1 and 2 by aceclofenac in whole blood assays, with selectivity for COX-2 being evident.

In contrast to some other NSAIDs, aceclofenac has shown stimulatory effects on cartilage matrix synthesis, that may be linked to the ability of the drug to inhibit IL-1 [illegible] data activity in vitro. ulation by the drug of synthesis of glycosaminoglycan in osteoarthritic cartilage. There is also evidence that aceclofenac stimulates the synthesis of IL-1 receptor antagonist in human articular chondrocytes subjected to inflammatory stimuli and that 4'-hydroxyaceclofenac has chondroprotective properties attributable to suppression of IL-1 mediated promatrix metalloproteinase production and proteoglycan release.

In patients with osteoarthritis of the knee, aceclofenac decreases pain, reduces disease severity and improves the functional capacity of the knee. It reduces joint inflammation, pain intensity and the duration of morning stiffness in patients with rheumatoid arthritis. The duration of morning stiffness and pain intensity are reduced and spinal mobility improved, by aceclofenac in patients with ankylosing spondylitis.

5.2. Pharmacokinetic Properties

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 glucoronides 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.

5.3. Preclinical Safety Data

Carcinogenic studies in the mouse (systemic exposure to aceclofencac unknown and in the rat (metabolism to diclofenac) did not show any carcinogenic effects and aceclofenac was negative in genotoxicity tests.

Animal studies indicate that there was no evidence of teratogenesis in rats although the systemic exposure was low and in rabbits, treatment with aceclofenac (10 mg/kg/day) resulted in a series of morphological changes in some foetuses.

6. PHARMACEUTICAL PARTICULARS:

6.1 List of excipients:

Microcrystalline Cellulose BP, Croscarmellose Sodium BP, Sodium Starch Glycollate BP, Colloidal Anhydrous Silica BP, Sodium Lauryl Sulphate BP,Hypromellose BP,Polyoxyl-40 Hydrogenated Castor Oil USP-NF, Isopropyl Alcohol BP, Methylene Chloride EP, Pregelatinised Starch BP, Sodium Metabisulphite BP, Sodium Methyl Hydroxybenzoate BP, Sodium Propyl Hydroxybenzoate BP, Purified Water BP, Purified Talc BP, Stearic Acid BP, Titanium Dioxide BP, Dibutyl Phthalate BP ,Ferric Oxide Yellow USP-NF

6.2 Incompatibilities:

No incompatibilities are known

6.3 Shelf – life:

24 months

6.4 Special precautions for storage:

Store below 30°C in a dry place.

Keep out of reach of children

6.5 Nature and contents of container:

Blister strip of 3 tablets. 10 Such strips packed in a printed showbox along with leaflet.

6.6 Special precautions for disposal:

No data found

7.0 MARKETING AUTHORIZATION HOLDER:

Ipca Laboratories Ltd.

Regd. Off.: 48, Kandivli Ind. Estate,

Mumbai 400 067, India.

Phone : 91 –22- 66474444

Fax : 91-22 – 28686613

Email : ipca@ipca.co.in

8.0 MARKETING AUTHORIZATION HOLDER:

25/35/83

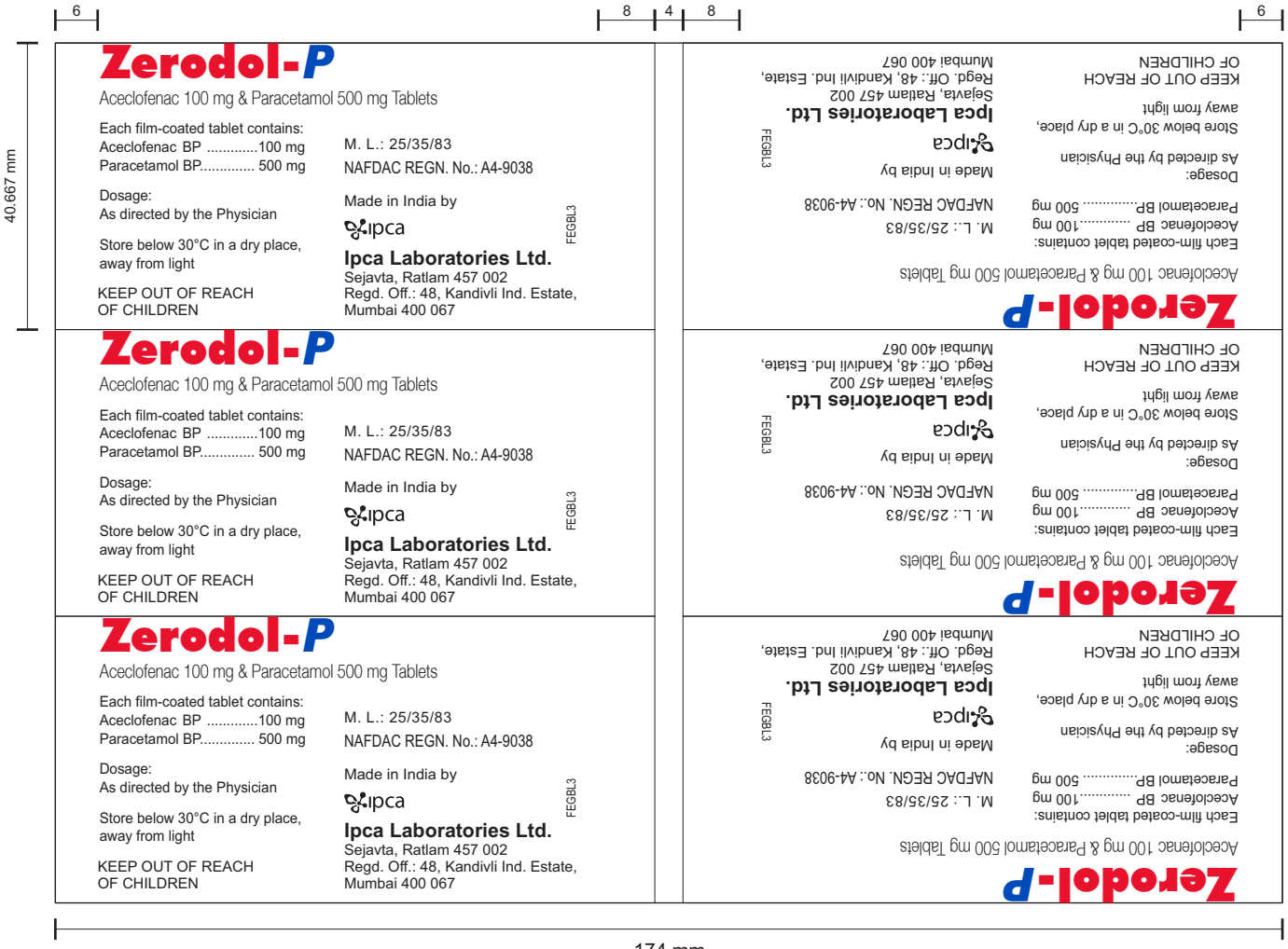
9.0 DATE OF FIRST AUTHORIZATION / RENEWAL OF AUTHORIZATION:

10.0 DATE OF REVISION OF TEXT:

Aug/2015

1.3.2 Labelling

Enclosed



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1.3.3 Package Insert

Enclosed

For the use only of a Registered Medical Practitioner or a Hospital or a Laboratory

Zerodol-*P*

Aceclofenac 100 mg & Paracetamol 500 mg Tablets

DESCRIPTION

Aceclofenac is an orally administered phenylacetic acid derivative with effects on a variety of inflammatory mediators. It is from the class of non-steroidal anti-inflammatory drug (NSAID), related to diclofenac.

Paracetamol is a non-opiate, non-salicylate analgesic and antipyretic.

COMPOSITION

Each film-coated tablet contains:

Aceclofenac BP ..... 100 mg

Paracetamol BP ..... 500 mg

PHARMACOLOGY

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 (COX), which is involved in the production of prostaglandins.

Aceclofenac has been shown to exert effects on a variety of mediators of inflammation. The drug inhibits synthesis of the inflammatory cytokines interleukin (IL)-1 and tumour necrosis factor and inhibits prostaglandin E_2 (PGE_2) production. Effects on cell adhesion molecules from neutrophils have also been noted. In vitro data indicate inhibition of COX-1 and 2 by aceclofenac in whole blood assays, with selectivity for COX-2 being evident.

Paracetamol

Paracetamol is a clinically proven analgesic and antipyretic. It produces analgesia by elevation of the pain threshold and antipyresis through action on the hypothalamic heat regulating centers. It is almost as potent as aspirin in inhibiting prostaglandin synthetase in the central nervous system (CNS) but its peripheral inhibition of prostaglandin synthesis is minimal, which may account for its lack of clinically significant antirheumatic or anti-inflammatory effects.

Paracetamol may act predominantly by inhibiting prostaglandin synthesis in the CNS and to a lesser extent, through a peripheral action by blocking pain impulse generation. The peripheral action may also be due to inhibition of prostaglandin synthesis or to inhibition of the synthesis or actions of other substances that sensitize pain receptors to mechanical or chemical stimulation.

Paracetamol produces antipyresis by acting centrally on the hypothalamic heat-regulating center to produce peripheral vasodilation resulting in increased blood flow through the skin, sweating and heat loss. The central action probably involves inhibition of prostaglandin synthesis in the hypothalamus.

PHARMACOKINETICS

Aceclofenac

Aceclofenac is rapidly and completely absorbed after oral administration. Peak plasma concentrations are reached 1 to 3 hours after an oral dose. The drug is highly protein bound (>99%). The presence of food does not alter the extent of absorption of aceclofenac but the absorption rate is reduced. The plasma concentration of aceclofenac was approximately twice that in synovial fluid after multiple doses of the drug in patients with knee pain and synovial fluid effusion.

Aceclofenac is metabolised to a major metabolite, 4'-hydroxyaceclofenac and to a number of other metabolites including 5-hydroxyaceclofenac, 4'-hydroxydiclofenac, diclofenac and 5-hydroxydiclofenac. These other metabolites account for the fate of approximately 20% of each dose of aceclofenac. Renal excretion is the main route of elimination of aceclofenac with 70 to 80% of an administered dose found in the urine, mainly as the glucuronides of aceclofenac and its metabolites. Of each dose of aceclofenac, 20% is excreted in the faeces. The plasma elimination half life of the drug is approximately 4 hours.

Paracetamol

Absorption of paracetamol is rapid and almost complete from the GI tract. Peak plasma concentrations occur within 10 to 60 minutes after oral administration. Paracetamol is distributed throughout most body tissues. About 25% of paracetamol in blood is bound to plasma proteins. The plasma half life is 1.25 to 3 hours but may be increased by liver damage and following overdosage. Paracetamol is metabolized in the liver. About 85% of a dose of paracetamol is excreted in urine as free and conjugated paracetamol within 24 hours.

INDICATIONS

The combination is indicated for:

Rheumatoid arthritis, osteoarthritis, ankylosing spondylitis, cervical spondylitis, intervertebral disc syndrome, sciatica, non-articular rheumatic conditions, post-operative and traumatic inflammations and painful inflammatory conditions in gynaecology and dentistry.

CONTRAINDICATIONS

The combination should not be administered to:

- patients hypersensitive to aceclofenac, paracetamol or other NSAIDs
- patients with a history of aspirin or NSAID- related allergic or anaphylactic reactions
- patients with peptic ulcers or GI bleeding, moderate or severe renal impairment
- patients with anemia or cardiac,pulmonary, renal or hepatic disease.

WARNINGS

Aceclofenac

- Close medical surveillance is imperative in patients with symptoms indicative of gastrointestinal disorders such as gastrointestinal bleeding or ulcerative perforation, haematemesis and melaena. These have in general more serious consequences in the elderly. They can occur at any time during treatment, with or without warning symptoms or previous history. In the rare instances, 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.
- As with other NSAIDs, allergic reactions, including anaphylactic/anaphylactoid reactions, can also occur without earlier exposure to the drug.

Paracetamol

Since chronic, excessive consumption of alcohol may increase the risk of paracetamol induced hepatotoxicity, chronic alcoholics should be cautioned to avoid regular or excessive use of paracetamol, or alternatively to avoid chronic ingestion of alcohol. Clinicians should be consulted by patients who generally consume 3 or more alcohol-containing drinks per day since paracetamol may increase the risk of hepatotoxicity.

PRECAUTIONS

Do not exceed the recommended dose of Zerodol-P

Aceclofenac

- 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.
- 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.
- Aceclofenac may trigger attacks in patients with hepatic porphyria, and reversible inhibition of platelet aggregation may occur with the drug.
- Refrain from driving or operating machinery if there is feeling of dizziness or sleepiness whilst taking aceclofenac. Do not perform any of these actions until the effects wear off.

Paracetamol

- The hazards of overdose are greater in those with (non-cirrhotic) alcoholic liver disease.
- Care is advised in the administration of paracetamol to patients with severe renal or severe hepatic impairment.
- Paracetamol should be used with caution in patients with preexisting anemia, since cyanosis may not be apparent despite dangerously high blood concentrations of methemoglobin.
- Although psychologic dependence on paracetamol may occur, tolerance and physical dependence do not appear to develop even with prolonged use.
- Severe or recurrent pain, high or continued fever may indicate serious illness. Underlying cause of persistent pain and inflammation should be investigated.

Usage in pregnancy and lactation

The combination is not recommended in pregnant or breast feeding women.

Usage in paediatrics

There are no clinical data on the use of the combination in children.

Usage in geriatrics

The pharmacokinetics of aceclofenac are not altered in elderly patients, therefore it is not considered necessary to modify the dose or dose frequency.

As with other non-steroidal anti-inflammatory drugs (NSAIDs), caution should be exercised in the treatment of elderly patients, who are generally more prone to adverse reactions, and who are more likely to be suffering from impaired renal, cardiovascular or hepatic function and receiving concomitant medication.

In the elderly, the rate and extent of paracetamol absorption is normal but plasma half life is longer and paracetamol clearance is lower than in young adults.

Drug interactions

- Drug interactions associated with aceclofenac are similar to those observed with other NSAIDs. Aceclofenac may increase plasma concentrations of lithium and digoxin, increase the activity of

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anticoagulants, inhibit the activity of diuretics, enhance cyclosporin nephrotoxicity and precipitate convulsions when coadministered 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 coadministration of aceclofenac with other NSAIDs or corticosteroids may result in increased frequency of adverse events.
- 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.

Paracetamol

- Since concomitant administration of paracetamol (especially when administered in high dosages or for prolonged periods) with oral anticoagulants may potentiate the effects of the oral anticoagulant, additional monitoring of prothrombin time (PT)/ international normalized ratio (INR) values has been suggested for patients receiving oral anticoagulants following initiation of, or during sustained therapy with, large doses of paracetamol.
- Since chronic, excessive consumption of alcohol may increase the risk of paracetamol-induced hepatotoxicity, chronic alcoholics should be cautioned to avoid regular or excessive use of paracetamol or alternatively to avoid chronic ingestion of alcohol.
- Anticonvulsants (including phenytoin, barbiturates, carbamazepine), isoniazid, rifampin and sulfinpyrazone that induce hepatic microsomal enzymes may increase paracetamol-induced liver toxicity.
- Propranolol appears to inhibit the enzyme systems responsible for the glucuronidation and oxidation of paracetamol. Therefore, the pharmacologic effects of paracetamol may be increased.
- On administration of activated charcoal or cholestyramine, absorption of paracetamol is reduced.
- With oral contraceptives, there is increase in glucuronidation resulting in increased plasma clearance and a decreased half-life of paracetamol.
- Probenecid may increase the therapeutic effectiveness of paracetamol slightly. The absorption of paracetamol may be increased by metoclopramide or domperidone.
- When given concomitantly with lamotrigine, serum lamotrigine concentrations may be reduced, producing a decrease in therapeutic effects.
- The effects of the loop diuretic may be decreased because paracetamol may decrease renal prostaglandin excretion and decrease plasma renin activity.
- The pharmacologic effects of zidovudine may be decreased because of enhanced nonhepatic or renal clearance of zidovudine.

ADVERSE DRUG REACTIONS

Aceclofenac

Aceclofenac is well tolerated, with most adverse events being minor and reversible and affecting mainly the GI system.

Although the incidence of GI adverse events with aceclofenac was similar to those of comparator NSAIDs in individual clinical trials, withdrawal rates due to these events were significantly lower with aceclofenac than with ketoprofen and tenoxicam. Costs incurred as a result of adverse event management are lower with aceclofenac than with a range of comparator NSAIDs. Although statistical analyses were not consistently available, faecal bleeding and endoscopy studies in humans have indicated overall less GI bleeding and GI mucosal damage with aceclofenac than with naproxen or diclofenac.

The following adverse events (described as most frequent ≥5%, occasional < 5% or rare cases < 0.1%) were reported during all clinical trials:

Gastrointestinal disorders: Most frequent: dyspepsia, abdominal pain, Occasional: nausea, diarrhoea, flatulence, gastritis, constipation, vomiting, ulcerative stomatitis. Rare cases: pancreatitis, melaena, stomatitis

Central and peripheral nervous system: Occasional: dizziness, vertigo. Rare cases: paraesthesia, tremor

Psychiatric: Rare cases: depression, abnormal dreaming, somnolence, insomnia

Skin and appendages: Occasional: pruritus, rash, dermatitis. Rare cases: eczema

Liver and biliary: Occasional: hepatic enzymes increased

Metabolic: Occasional: BUN increased, blood creatinine increased. Rare cases: alkaline phosphatase increased, hyperkalaemia

Cardiovascular: Rare cases: oedema (dependent), palpitation, leg cramps, flushing, purpura

Respiratory: Rare cases: dyspnoea, stridor

Blood: Rare cases: anaemia, granulocytopenia, thrombocytopenia

Body as whole, general: Rare cases: headache, fatigue, face oedema, hot flushes, allergic reaction, weight increase

Other: Rare cases: abnormal vision, abnormal taste

Paracetamol

Paracetamol is relatively nontoxic in therapeutic doses.

Adverse reactions reported with paracetamol include:

Dermatologic: Pruritic maculopapular rash, skin eruptions, erythematous skin reactions and urticaria

Hypersensitivity: Laryngeal edema, angioedema and anaphylactoid reactions

Hematologic: Thrombocytopenia, anemia, leukopenia, pancytopenia, neutropenia thrombocytopenic purpura and agranulocytosis has been reported in patients receiving paracetamol. It does not normally produce methemoglobinemia or hemolysis, even after overdosage or in patients with dextrose-6-phosphate dehydrogenase deficiency. Nevertheless there have been isolated reports of these complications.

Renal: Renal colic, renal failure (sudden decrease in amount of urine), sterile pyuria (cloudy urine). Nephrotoxicity following therapeutic doses of paracetamol is uncommon but papillary necrosis has been reported after prolonged administration.

Respiratory: Paracetamol may very rarely aggravate bronchospasm in patients who are sensitive to aspirin and other non-steroidal anti-inflammatory drugs.

Liver: Hepatotoxicity and jaundice. Hepatotoxicity can result from ingestion of single toxic dose or multiple excessive doses of paracetamol.

Miscellaneous: Hypoglycemic coma

DOSAGE AND ADMINISTRATION

The usual dose is one tablet given twice daily by mouth. One tablet in the morning and one in the evening.

There is no evidence that the dosage of aceclofenac needs to be modified in patients with mild renal impairment, but as with other NSAIDs caution should be exercised.

There is some evidence that the dose of aceclofenac should be reduced in patients with hepatic impairment and it is suggested that an initial daily dose of 100mg be used.

The tablets should be swallowed whole with a sufficient quantity of liquid. When aceclofenac was administered to fasting and fed healthy volunteers only the rate and not the extent of aceclofenac absorption was affected and as such aceclofenac can be taken with food.

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, gastrointestinal irritation, and respiratory depression, specific therapies such as forced diuresis, dialysis or haemoperfusion are probably of no help in eliminating NSAIDs due to their high rate of protein binding and extensive metabolism.

Paracetamol

In paracetamol overdosage, dose dependent, potentially fatal hepatic necrosis is the most serious adverse effect. Renal tubular necrosis, hypoglycemic coma and thrombocytopenia may also occur.

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. Other symptoms may be drowsiness, confusion, liver tenderness, low blood pressure, cardiac arrhythmias, jaundice and acute hepatic and renal failure.

In adults, hepatic toxicity has rarely been reported with acute overdoses of less than 10g or fatalities with less than 15g.

If the dose of paracetamol may have exceeded 140mg/Kg, acetylcysteine should be administered as early as possible. Serum paracetamol levels should be obtained, since levels four or more hours following ingestion help predict paracetamol toxicity. Perform gastric lavage in all cases. Do not await paracetamol assay results before initiating treatment. Hepatic enzymes should be obtained initially and repeated at 24 hour intervals.

Methemoglobinemia over 30% should be treated with methylene blue by slow intravenous administration.

The toxic dose for adults for paracetamol is 10g.

PRESENTATION

Blister strip of 2, 4 & 10 tablets

STORAGE

Store below 30°C in a dry place, away from light

KEEP OUT OF REACH OF CHILDREN

Made in India by

Ipca

Ipca Laboratories Ltd.
Regd. Off.: 48, Kandivli Ind. Estate,
Mumbai 400 067

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