1. NAME OF THE MEDICINAL PRODUCT

Aceclofenac and Paracetamol Tablet

2. QUALITATIVE AND QUANTITATIVECOMPOSITION

Each film coated tablet contains:
Aceclofenac BP 100mg
Paracetamol BP 500mg
Excipients Q.S.
Colour: Titanium Dioxide, Sunset Yellow Lake and Tartrazine Yellow

3. PHARMACEUTICAL FORM

Oral Film coated tablets

4. Clinical particulars

4.1 Therapeutic indications

ACECLOFENAC AND PARACETAMOL TABLETS isindicated for relief from 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.

4.2 Posology and method of administration

ACECLOFENAC AND PARACETAMOL TABLETStablets are supplied for oral administration in adults. The maximum recommended dose of ACECLOFENAC AND PARACETAMOL TABLETSis two tablets daily, taken as one tablet in the morning and one in the evening.

4.3 Contraindications

ACECLOFENAC AND PARACETAMOL TABLETSis contraindicated in the following situations:

- 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 precautions for use

ACECLOFENAC AND PARACETAMOL TABLETSmay cause dizziness. Driving or operating machineries are to be avoided.
Individuals receiving long-term treatment should be regularly monitored for renal unction tests, liver function tests and blood counts. It is to be used with caution n 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.

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 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, 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 coadministered with probenecid. Cholestyramine also reduces the absorption of Paracetamol.

4.6 Pregnancy and Lactation

Pregnancy: The drug in not recommended in pregnant women.
Lactation: The drug in not recommended in breast-feeding women.

4.7 Effects on ability to drive and use machines

Information not available

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 also occur with ACECLOFENAC AND PARACETAMOL TABLETS.

4.9 Overdose

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

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamics properties

Paracetamol (INN) is a widely used analgesic and antipyretic drug that is used for the relief of fever, headaches, and other minor aches and pains. It is a major ingredient in numerous cold and flu medications and many prescription analgesics. It is extremely safe in standard doses, but because of its wide availability, deliberate or accidental overdoses are not uncommon. Paracetamol, unlike other common analgesics such as aspirin and ibuprofen, has no anti-inflammatory properties or effects on platelet function, and it is not a member of the class of drugs known as non-steroidal anti-inflammatory drugs or NSAIDs. At therapeutic doses Paracetamol does not irritate the lining of the stomach nor affect blood coagulation, kidney function, or the fetal ductus arteriosus (as NSAIDs can). Like NSAIDs and unlike opioid analgesics, acetaminophen does not cause euphoria or alter mood in any way. Paracetamol and NSAIDs have the benefit of being completely free of problems with addiction, dependence, tolerance and withdrawal. Paracetamol is used on its own or in combination with pseudoephedrine, dextromethorphan, chlorpheniramine, diphenhydramine, doxylamine, codeine, hydrocodone, or oxycodone.
Paracetamol is an acetic acid nonsteroidal antiinflammatory drug (NSAID) with analgesic and antipyretic properties. Paracetamol is used to treat pain, dysmenorrhea, ocular inflammation, osteoarthritis, rheumatoid arthritis, ankylosing spondylitis, and actinic keratosis
Mechanism of Action
Paracetamol is thought to act primarily in the CNS, increasing the pain threshold by inhibiting both isoforms of cyclooxygenase, COX-1, COX-2, and COX-3 enzymes involved in prostaglandin (PG) synthesis. Unlike NSAIDs, acetaminophen does not inhibit cyclooxygenase

in peripheral tissues and, thus, has no peripheral anti-inflammatory affects. While aspirin acts as an irreversible inhibitor of COX and directly blocks the enzyme's active site, studies have found that Paracetamol indirectly blocks COX, and that this blockade is ineffective in the presence of peroxides. This might explain why Paracetamol is effective in the central nervous system and in endothelial cells but not in platelets and immune cells which have high levels of peroxides. Studies also report data suggesting that Paracetamol selectively blocks a variant of the COX enzyme that is different from the known variants COX-1 and COX-2. This enzyme is now referred to as COX-3. Its exact mechanism of action is still poorly understood, but future research may provide further insight into how it works. The antipyretic properties of Paracetamol are likely due to direct effects on the heat-regulating centres of the hypothalamus resulting in peripheral vasodilation, sweating and hence heat dissipation.
The antiinflammatory effects of Aceclofenac are believed to be due to inhibition of both leukocyte migration and the enzyme cylooxygenase (COX-1 and COX-2), leading to the peripheral inhibition of prostaglandin synthesis. As prostaglandins sensitize pain receptors, inhibition of their synthesis is responsible for the analgesic effects of Aceclofenac. Antipyretic effects may be due to action on the hypothalamus, resulting in peripheral dilation, increased cutaneous blood flow, and subsequent heat dissipation.

5.2 Pharmacokinetic properties

Aceclofenac: Rapidly absorbed; almost 100% bioavailability; peak plasma levels reached about 1.25-3 hours after oral admin.

Distribution
Aceclofenac: >99.7% bound to plasma proteins; distributes into synovial fluid. Paracetamol: Distributes throughout most fluids of the body.

Metabolism
Aceclofenac: Probably metabolised by CYP2C9; average plasma elimination half-life: 4-4.3 hours. Paracetamol: Mainly metabolised hepatically; plasma elimination half-life: 1-4 hours.

Excretion
Aceclofenac: About two-thirds of the administered dose is removed in the urine, mainly as conjugated hydroxymetabolites. Paracetamol: Most metabolites are removed in the urine within 24 hours.

5.3 Preclinical safety data

None stated.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Povidone K-30 BP
Maize Starch BP
Sodium Benzoate BP
Purified Talc BP
Magnesium Stearate BP
Sodium Starch Glycolate BP
Colloidal Anhydrous Silica BP
Colorezy White 17F580001 IH
Lake of Sunset Yellow IH
Lake of Tartrazine IH
Isopropyl Alcohol BP
Methylene Chloride BP
Purified Water BP

6.2 Incompatibilities

Not applicable

6.3 Shelf life

36 months for the date of manufacturing.

6.4 Special precautions for storage

Store at a temperature not exceeding 30ºC in a dry place. Protect from light. Keep out of reach of children.

6.5 Nature and contents of container<and special equipment for use, administration or implantation>

2 X 10 Tablets Alu-Alu Blister Pack

6.6 Special precautions for disposal <and other handling>

There are no special storage precautions. Any unused product or waste material should be disposed of in accordance with local requirements.

7 <APPLICANT/MANUFACTURER>

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