ZULU-P

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

Abbreviated Prescribing information for ZULU P (Aceclofenac and Paracetamol Tablets I.P)
[Please refer the complete prescribing information available at www.torrentpharma.com]

PHARMACOLOGICAL PROPERTIES:

MECHANISM OF ACTION: *Aceclofenac:* The mode of action of aceclofenac is largely based on the inhibition to prostaglandin synthesis. Aceclofenac is a potent inhibitor of the enzyme cyclo-oxygenase, which is involved in the production of prostaglandins. *Paracetamol:* Analgesic – the mechanism of analgesic action has not been fully determined. Paracetamol may act predominantly by inhibiting prostaglandin synthesis in the central nervous system (CNS) and to a lesser extent, through a peripheral action by blocking pain impulse generation.

INDICATIONS: For acute painful conditions in adults only.

DOSAGE AND ADMINISTRATION: *Dosage*: As directed by the Physician. *Mode of Administration*: The tablet must be taken orally, swallowed whole with liquid and may be taken with or without food. It is recommended to take the daily dose in one single intake. Never change the dose of your medicine without talking to your doctor first

CONTRAINDICATION: Hypersensitivity to the active substance Aceclofenac and Paracetamol, or to any of the other excipients ; Active, or history of recurrent peptic ulcer/haemorrhage (two or more distinct episodes of proven ulceration or bleeding) ; NSAIDS are contraindicated in patients who have previously shown hypersensitivity reactions (eg. Asthma, rhinitis, angioedema or urticaria) in response to ibuprofen, aspirin, or other non-steroidal anti-inflammatory drugs ; Hepatic failure and renal failure ; Patients with established congestive heart failure (NYHA II-IV), ischaemic heart disease, peripheral arterial disease and/or cerebrovascular disease ; History of gastrointestinal bleeding or perforation, related to previous NSAIDS therapy ; Active bleedings or bleeding disorders ; Aceclofenac should not be prescribed during pregnancy, especially during the last trimester of pregnancy ; unless there are compelling reasons for doing so. The lowest effective dosage should be used.

WARNINGS & PRECAUTIONS: Not for veterinary use, Taking more than daily dose may cause serious liver damage or allergic reactions (e.g. Swelling of the face, mouth and throat, difficulty in breathing, itching or rash). *Respiratory disorders:* Caution is required if administered to patients suffering from, or with a previous history of, bronchial asthma since NSAIDs have been reported to precipitate bronchospasm in such patients. *Renal and Hepatic Impairment:*The administration of an NSAID may cause a dose dependent reduction in prostaglandin formation and precipitate renal failure. Patients at greatest risk of this reaction are those with impaired renal function, cardiac impairment, liver dysfunction, those taking diuretics or recovering from major surgery, and the elderly. *Renal:* Patients with mild to moderate renal impairment should be kept under surveillance, since the use of NSAIDs may result in deterioration of renal function. *Hepatic:* If abnormal liver function tests persist or worsen, clinical signs or symptoms consistent with liver disease develop or if other manifestations occur (eosinophilia, rash), Aceclofenac Tablets should be discontinued. *Cardiovascular and cerebrovascular effects*: Appropriate monitoring and advice are required for patients with a history of hypertension and/or mild to moderate congestive heart failure as fluid retention and oedema have been reported in association with NSAID therapy. *Dermatological:* Serious skin reactions, some of them fatal, including exfoliative dermatitis, Stevens-Johnson syndrome, and toxic epidermal necrolysis, have been reported very rarely in association with the use of NSAIDs. *Hypersensitivity reactions:* As with other NSAIDs, allergic reactions, including anaphylactic/anaphylactoid reactions, can also occur without earlier exposure to the drug. *Haematological:* Aceclofenac Tablets may reversibly inhibit platelet aggregation (see under 'Interactions').*Paracetamol* Taking multiple daily doses in one administration can severely damage the liver; in such case unconsciousness does not occur. However, medical assistance should be sought immediately. Prolonged use except under medical supervision may be

harmful. In children treated with 60mg/kg daily of Paracetamol, the combination with another antipyretic is not justified except in the case of ineffectiveness. The hazards of overdose are greater in those with non-cirrhotic alcoholic liver disease. Caution should be exercised in cases of chronic alcoholism. The daily dose should not exceed 2000 mg in such case.Alcohol should not be used during the treatment with Paracetamol."Caution is advised in asthmatic patients sensitive to aspirin, because light reaction bronchospasm with paracetamol (cross-reaction) has been reported in less than 5% of the patients tested" Abrupt discontinuation of long term use of high-dosed analgesics, taken not as directed, may cause headache, tiredness, muscular pain, nervousness and vegetative symptoms. The withdrawal symptoms subside within a few days. Patients should be advised to consult their doctor if headaches become persistent. Paracetamol Effervescent Tablets should not be administered in children and adolescents below 16 years of age and under 50 kg body weight. This medicinal product contains 438 mg of sodium per tablet. To be taken into consideration by patients on a controlled sodium diet. Do not exceed the stated dose Treatment with an antidote is advised if an overdose is suspected.

DRUG INTERACTIONS: *Aceclofenac- Anti-hypertensives*: NSAIDs, may reduce the effect of activity antihypertensives. *Diuretics:* Aceclofenac, like other NSAIDs, may inhibit the activity of diuretics. *Cardiac glycosides like digoxin*: NSAIDs may exacerbate cardiac failure, reduce GFR (glomerular filtration rate) and inhibit the renal clearance of glycosides, resulting in increased plasma glycoside levels. *Lithium*: Several NSAID drugs inhibit the renal clearance of lithium, resulting in increased serum concentrations of lithium. *Methotrexate:* The possible interaction between NSAIDs and methotrexate should be born in mind also when low doses of methotrexate are used, especially in patients with decreased renal function. *Mifepristone:* NSAIDs should not be used for 8-12 days after mifepristone administration as NSAIDs can reduce the effect of mifepristone. C*orticosteroids*: Increased risk of gastrointestinal ulceration or bleeding. *Anti-coagulants:* NSAIDs may enhance the effects of anti-coagulants, such as warfarin. Close monitoring of patients on combined anti-coagulants and Aceclofenac Tablets therapy should be undertaken. *Quinolone antibiotics*: Animal data indicate that NSAIDs can increase the risk of convulsions associated with quinolone antibiotics. *Anti-platelet agents and selective serotonin reuptake inhibitors (SSRIs):* Increased risk of gastrointestinal bleeding. *Ciclosporin, Tacrolimus*: Administration of NSAID drugs together with ciclosporin or tacrolimus is thought to increase the risk of nephrotoxicity due to decreased synthesis of prostacyclin in the kidney. During combination therapy it is therefore important to carefully monitor renal function. *Zidovudine*: Increased risk of haematological toxicity when NSAIDs are given with zidovudine. *Antidiabetic agents:* Aceclofenac Tablets, consideration should be given to adjustment of the dosage of hypoglycaemic agents. *Paracetamol Probenecid* causes an almost 2-fold reduction in clearance of Paracetamol by inhibiting its conjugation with glucuronid acid. A reduction of the Paracetamol dose should be considered for concomitant treatment with probenecid.*Salicylamid*e may prolong the elimination t1/2 of Paracetamol. *Metoclopramide and donperidone* accelerate absorption of Paracetamol. *Cholestyramine* reduces absorption of Paracetamol and therefore should not be administered within an hour following Paracetamol administration. Concomitant use of Paracetamol (4000 mg per day for at least 4 days) with *oral anticoagulants* may lead to slight variations of INR values. *Isoniazid:* Reduction of paracetamol clearance, with possible potentiation of its action and/or toxicity, by inhibiting its metabolism in the liver. *Lamotrigine:* decrease in the bioavailability of lamotrigine, with possible reduction of its effect, due to possible induction of liver metabolism. *Interference with laboratory tests*:Paracetamol may affect uric acid tests by wolframatop phosphoric acid, and blood sugar tests by glucose-oxidase-peroxidase.

ADVERSE REACTIONS:. *Aceclofenac-Common (may affect up to 1 in 10 people):* dizziness,nausea, diarrhoea,increased liver enzymes in the blood, *Uncommon (may affect up to 1 in 100 eople):*ind,inflammation or irritation of the lining of the stomach,constipation,vomiting,mouth ulcers, itching,rash,inflammation of the skin, raised circular red itchy, stinging or burning patches on the skin (hives), increase in blood urea levels,increase in blood creatinine levels,*Rare (may affect up to 1 in 1,000 people):* hypersensitivity (allergic reaction,)problems with eyesight, heart failure, high blood pressure shortness of breath , bleeding from the stomach or bowel,stomach or bowel ulceration,*Very Rare (may affect up to 1 in 10,000 people):* depression, strange dreams, inability to sleep, tingling, pricking or numbness of

skin, uncontrollable shaking,drowsiness, headaches,abnormal taste in the mouth,sensation of spinning when standing still,ringing in the ears,heart pounding or racing hot flushes,difficulty breathing,high pitched noise when breathing, inflammation of the mouth,perforation of either the stomach, large intestine or bowel wall,worsening of colitis and Crohn's disease,inflammation of the pancreas injury of the liver (including hepatitis),yellowing of the skin (jaundice), spontaneous bleeding into the skin (appears as a rash), nephrotic syndrome: a condition which indicates kidney damage and includes large amounts of protein in the urine, low blood albumin levels, high blood cholesterol levels and swelling of the legs, feet or ankles, water retention and swelling,tiredness,leg cramps,increased blood alkaline phosphatase levels, weight gain,*Other side effects that have been reported with this type of drug (NSAIDs) are:* hallucinations,confusion ,blurred, partial or complete loss of vision,painful movement of the eye,worsening of asthma,skin reaction to sunlight,inflammation of the kidneys,generally feeling unwell, *Paracetamol*-Bleeding problems or clotting disorders (Platelet disorders), decreased formation of cells, severe decrease in white blood cells which may lead to severe infections (agranulocytosis), frequent infections due to poorly functioning white blood cells or decrease in white blood cells (leucopenia), reduction in blood platelets, which increases the risk of bleeding or bruising (thrombocytopenia) abnormal breakdown of red blood cells, which may cause weakness or pale skin (haemolytic anaemia), decrease in blood count (pancylopenia), reduced neutrophil count in blood (neutropenia).Allergies (excludig swelling on the face, mouth, hands),Depression, confusion, sensing unreal things,Tremor, headache,Abnormal vision,Abnormal accumulation of fluid under the skin (oedema),Stomach pain, diarrhoea, nausea (feeling sick), vomiting or bleeding (haemorMage),Abnormal liver function, liver failure, death of liver cells (hepatic necrosis), jaundice,Dizziness, feeling of general discomfort or uneasiness (malaise), fever, drowsiness, drug interaction,Overdose and poisoning,Damage caused to the liver (hepatotoxicity),Immediate severe allergic reaction (hypersensitivity reaction requiring discontinuation of treatment),Low levels of glucose in the blood (hypoglycemia),Cloudy urine and kidney disorders,Life-threate ning skin disease causing rash, skin peeling and sores (epidermal necrolysis),Allergic reaction of the skin (erythema multiforme),Severe life-threatening skin disease causing rash, skin peeling, sores (Stevens-Johnson syndrome),Accumulation of fluid in the voice box (larynx).Severe allergic reaction (anaphylactic shock),Decrease in red blood cells (anemia),Severe kidney impairment (renal alteration),Kidney disorder (nephrite interstitial),Blood in urine (haematuria),Inability to urinate (anuresis),Stomach ulcers and bleeding (gastrointestinal effects),and Uneasiness. .

MARKETED BY:

TORRENT PHARMACEUTICALS LTD.

IN/ZULU-P/100, 325 mg/SEP-24/04/PI

(Additional information is available on request)