1.17 SUMMARY OF THE PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Trade Name: ZYRTAL PLUS
Generic Name: Paracetamol and Aceclofenac Tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Esostar-20

Each Film coated tablet contains:
Paracetamol BP 500mg
Aceclofenac BP -100mg
Colour : Titanium dioxide

For Excipients see 6.1

3. PHARMACEUTICAL FORM

Film coated Tablet.

4. CLINICAL PARTICULARS

Therapeutic indications
ZYRTAL PLUS is indicated 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.

Posology and method of administration

The recommended dose of ZYRTAL PLUS 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.
Keep out of reach of children.

Mode of Administration: Oral

Contraindications

ZYRTAL PLUS is 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

Precautions

ZYRTAL PLUS 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.

Interactions 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, 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.

Pregnancy and lactation
UPRIGHT during pregnancy and lactation should be avoided, unless the potential benefits outweigh the risks.

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.

Effects on ability to drive and use machines
No effects have been observed.

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

Pharmacodynamic properties
Mechanism of action

Aceclofenac relieves pain and inflammation through a variety of mechanisms and in addition exerts stimulatory effects on cartilage matrix synthesis.

Anti-inflammatory activity: The anti-inflammatory effects of Aceclofenac have been shown in both acute and chronic inflammation. It inhibits various mediators of pain and inflammation including:
• PGE2 via cyclooxygenase inhibition (COX-1 & COX-2) after intracellular metabolism to 4' hydroxy-aceclofenac and diclofenac in human rheumatoid synovial cells and other inflammatory cells. • IL-1β, IL-6 and tumor necrosis factor in human osteoarthritic synovial cells and human articular chondrocytes.
• Reactive oxygen species (which plays a role in joint damage) has also been observed in patients with osteoarthritis of knee.
• Expression of cell adhesion molecules (which is implicated in cell migration and inflammation) has also been shown in human neutrophils.
Stimulatory effects on cartilage matrix synthesis: Aceclofenac stimulates glycosaminoglycan synthesis in human osteoarthritic cartilage by inhibition of IL-1β and suppresses cartilage degeneration by inhibiting IL-1β mediated promatrix metalloproteinase production and proteoglycan release.

Paracetamol is a clinically proven analgesic and antipyretic agent with weak anti-inflammatory effect.

Analgesic action: The central analgesic action of Paracetamol resembles that of aspirin. It produces analgesia by raising pain threshold.
Antipyretic effect: The antipyretic effect of Paracetamol is attributed to its ability to inhibit COX in the brain where peroxide tone is low. Recent evidence suggests inhibition of COX-3 (believed to be splice variant product of the COX-1 gene) could represent a primary central mechanism by which Paracetamol decreases pain and possibly fever.

Pharmacokinetic properties
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.

SPECIAL POPULATION

As with other NSAIDs and combinations, caution is advised in elderly patients who are more likely to have concomitant renal, hepatic or cardiovascular impairment or receiving concurrent medication. In patients with hepatic impairment, dosage reductions are recommended. ZYRTAL PLUS should be avoided in patients with moderate and severe renal impairment. Regular use of ZYRTAL PLUS during pregnancy and lactation should be avoided, unless the potential benefits outweigh the risks.

5.3 Preclinical safety data

The results from preclinical studies conducted with aceclofenac are consistent with those expected for NSAIDs. The principal target organ was the gastro-intestinal tract.No unexpected findings were recorded.

Aceclofenac was not considered to have any mutagenic activity in three *in vitro* studies and an *in vivo* study in the mouse.

Aceclofenac was not found to be carcinogenic in either the mouse or rat.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Maize starch
Microcrystalline cellulose
Povidone
Sodium propyl hydroxyl Benzoate
Purified water
Purified Talc
Magnesium stearate
Croscarmellose sodium
Colloidal silicon dioxide
Hydroxy propyl methyl cellulose
Methylene chloride
Titanium dioxide
Isopropyl alcohol

6.2 Incompatibilities

None

6.3 Shelf-life

24 months from the date of manufacturing.

6.4 Special precautions for storage

Store below 30 °C. Protect from light and moisture.

6.5 Nature and contents of container

ZYRTAL PLUS is packed in Alu-Alu strip of Cold Forming Alu foil sealed with printed Aluminum foil on heat seal lacquer. Each Alu-Alu strip contains 10 tables. Such 2 blister strips and product information leaflet are packed in carton.

7. MARKETING AUTHORIZATION HOLDER

PHARMAKEN
P.O. BOX NO.95625 -80106
MOMBASA
5TH Floor , Links Plaza , Links Road Nyali
Mombasa
Country: KENYA

8. MARKETING AUTHORIZATION NUMBER

NOT APPLICABLE

9. DATE OF FIRST AUTHORISATION / RENEWAL OF THE AUTHORISATION

NOT APPLICABLE

10. DATE OF REVISION OF TEXT

NOT APPLICABLE