ACEPAR PLUS®
(Aceclofenac and Thiocolchicoside Tablet)

Qualitative and quantitative composition:
Each film coated tablet of Acepar plus contains: Aceclofenac BP 100 mg and Thiocolchicoside 4 mg
Each film coated tablet of Acepar plus DS contains: Aceclofenac BP 100 mg and Thiocolchicoside 8 mg
Excipients:
Microcrystalline cellulose, PVP–K 30 , Maize Starch, Sodium starch glycollate, Sodium Lauryl Sulphate, Purified talc, Magnesium Stearate, Purified water, Hypromellose, Titanium dioxide, Propylene glycol, Dichloromethane, Isopropyl alcohol & Lake of Sunset Yellow.
Pharmaceutical form: Acepar plus: Orange, circular, biconvex, film coated tablets, plain on both sides
Acepar plus DS: Orange capsule shaped film coated tablets plain on both sides.
Pharmacology
ATC Code: – Aceclofenac: M01AB16, Thiocolchicoside: M03BX05
Pharmacotherapeutic group: Anti-inflammatory, antirheumatic and muscle relaxant.
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. Through its analgesic and anti-inflammatory properties, aceclofenac provides symptomatic relief in a variety of painful conditions. Thiocolchicoside, a semi-synthetic derivative of the naturally occurring compound colchicoside with a relaxant effect on skeletal muscle, has been found to displace both [3H] gamma-amino butyric acid ([3H]GABA) and [3H]strychnine binding, suggesting an interaction with both GABA and strychnine-sensitive glycine receptors.
Pharmacokinetics:
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 litres. 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. Thiocolchicoside: After oral administration, no thiocolchicoside is detected in plasma. Only two metabolites are observed:- the pharmacologically active metabolite SL18.0740 and an inactive metabolite SL59.0955. For both metabolites, maximum plasma concentrations occur 1hour after thiocolchicoside administration.
After a single oral dose of 8 mg of thiocolchicoside the Cmax and AUC of SL18.0740 are about 60 ng/mL and 130 ng.h/mL respectively. For SL59.0955 these values are much lower: Cmax around 13 ng/mL and AUC ranging from 15.5 ng.h/mL (until 3h) to 39.7 ng.h/mL (until 24h). Thiocolchicoside is first metabolized into aglycon 3-demethyltiocolchicine. This step mainly occurs by intestinal metabolism explaining the lack of circulating unchanged thiocolchicoside by this route of administration. Aglycon 3-demethyltiocolchicine is then glucuroconjugated into SL18.0740 which has equipotent pharmacological activity to thiocolchicoside and thus supports the pharmacological activity after oral administration of thiocolchicoside. SL59.0955 is also demethylated into didemethyl-thiocolchicine. The metabolites are mainly excreted in feces (79%) while urinary excretion represents only 20%. No unchanged thiocolchicoside is excreted either in urine or feces.
Therapeutic indications:
Aceclofenac and Thiocolchicoside Tablets are indicated for the relief of pain and inflammation in osteoarthritis, rheumatoid arthritis and ankylosing spondylitis, Adjuvant treatment of painful muscle contractures in acute spinal pathology in adults 18 years and above.
Posology and method of administration:
Route of administration: Oral administration.
Dosing Adults: The recommended dose is one tablet twice daily. preferably with or after food..
Contraindications:
Hypersensitivity to Aceclofenac, Thiocolchicoside or to NSAIDs.
Severe heart failure, hepatic failure and renal failure.
History of gastrointestinal bleeding or perforation, related to previous NSAIDS therapy.
Tablets should not be prescribed during pregnancy, lactation and in women of childbearing potential not using contraception.
Special warnings and precautions for use:
The use of Aceclofenac with concomitant NSAIDs including cyclooxygenase - 2 selective inhibitors should be avoided.
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.
Cardiovascular, 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 and the elderly. Renal function should be monitored in these patients. Gastrointestinal bleeding, ulceration and perforation: GI bleeding, ulceration or perforation, which can be fatal, has been reported with all NSAIDs at any time during treatment, with or without warning symptoms or a previous history of serious GI events.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. Impaired female fertility: The use of Aceclofenac may impair female fertility and is not recommended in women attempting to conceive. In women who have difficulties conceiving or who are undergoing investigation of infertility, withdrawal of Aceclofenac should be considered. Preclinical studies showed that one of Thiocolchicoside metabolites induced aneuploidy (i.e. unequal number of chromosomes in dividing cells) at concentrations close to human exposure observed at doses 8 mg twice daily. Aneuploidy is considered as a risk factor for teratogenicity, embryo/foeto-toxicity, spontaneous abortion, and impaired male fertility and a potential risk factor for cancer..
Interaction with other medicinal products
Other analgesics including cyclooxygenase-2 selective inhibitors: Avoid concomitant use of two or more NSAIDs (including aspirin) as this may increase the risk of adverse effects.
Anti-hypertensives: NSAIDs may reduce anti-hypertensive effect.
Diuretics: NSAIDs may reduce the diuretic effect. Diuretics can increase the risk of nephrotoxicity of NSAIDs.
Cardiac glycosides: NSAIDs may exacerbate cardiac failure, reduce GFR (glomerular filtration rate) and increase plasma glycoside levels.
Lithium: NSAIDs decrease elimination of lithium.
Methotrexate: NSAIDs decrease elimination of methotrexate. Caution should be exercised if NSAIDs and methotrexate are administered within 24 hours of each other, since NSAIDs may increase plasma levels, resulting in increased toxicity.
Cyclosporine: Increased risk of nephrotoxicity.
Mifepristone: NSAIDs should not be used for 12 days after mifepristone administration as NSAIDs can reduce the effect of mifepristone.
Corticosteroids: concomitant use with NSAIDs increases risk of gastrointestinal ulceration or bleeding.
Anti-coagulants: NSAIDs may enhance the effects of anti-coagulants, such as warfarin.
Anti-platelet agents and selective serotonin reuptake inhibitors (SSRIs): Concomitant use with NSAIDs increases risk of gastrointestinal bleeding.
Tacrolimus: Possible increased risk of nephrotoxicity when NSAIDs are given with tacrolimus.
Other NSAIDs: Concomitant therapy with aspirin or other NSAIDs may increase the frequency of adverse reactions, including the risk of GI bleeding..
Pregnancy and lactation:
Pregnancy: Congenital abnormalities have been reported in association with NSAID administration; however, these are low in frequency and do not appear to follow any discernible pattern. In view of the known effects of NSAIDs on the foetal cardiovascular system (risk of closure of the ductusarteriosus) and on the possible risk of persistent pulmonary hypertension of the new born, use in the last trimester of pregnancy is contraindicated. There are limited data on the use of thiocolchicoside in pregnant women. Studies in animals have shown teratogenic effects.
Lactation: In limited studies so far available, NSAIDs can appear in breast milk in very low concentrations. NSAIDs should, if possible, be avoided when breastfeeding.
Thiocolchicoside passes into the mother's milk, the use of thiocolchicoside is contraindicated during breastfeeding
Effects on ability to drive and use machines: No effect on ability to drive and use machines.
Undesirable effects:
Gastrointestinal: The most commonly-observed side effects are gastrointestinal in nature. Peptic ulcers, perforation or GI bleeding, sometimes fatal, particularly in the elderly, may occur. Nausea, vomiting, diarrhoea, flatulence, constipation, dyspepsia, abdominal pain, melaena, haematemesis, ulcerative stomatitis, exacerbation of colitis and Crohn's disease have been reported following administration.
Less frequently, gastritis has been observed. Pancreatitis has been reported very rarely.
Hypersensitivity: Hypersensitivity reactions have been reported following treatment with NSAIDs. These may consist of non-specific allergic reactions and anaphylaxis, respiratory tract reactivity comprising asthma, aggravated asthma, bronchospasm or dyspnoea, or assorted skin disorders, including rashes of various types, pruritus, urticaria, purpura, angiodema and, more rarely exfoliative and bullous dermatoses (including epidermal necrolysis and erythema multiforme).
Cardiovascular: Oedema, hypertension and cardiac failure have been reported in association with NSAIDs treatment.
Overdose:
Symptoms: Symptoms include headache, nausea, vomiting, epigastric pain, gastrointestinal irritation, gastrointestinal bleeding, rarely diarrhoea, disorientation, excitation, coma, drowsiness, dizziness, tinnitus, hypotension, respiratory depression, fainting, occasionally convulsions. In cases of significant poisoning acute renal failure and liver damage are possible. Therapeutic measure: Patients should be treated symptomatically as required. Within one hour of ingestion of a potentially toxic amount, activated charcoal should be considered. Alternatively, in adults, gastric lavage should be considered within one hour of ingestion of a potentially life-threatening overdose.
Shelf life: 36 months from the date of manufacture.
Special precautions for storage:
Store below 30°C, Protected from light and moisture.
Keep all medicines out of reach of children.
Nature and contents of container:
Blister pack of 1x10's in unit boxes.
Legal category: Prescription Only Medicine.(POM)
Manufactured by:

DAWA Limited, Plot No. 7879/8, Baba Dogo Road, Ruaraka.
P. O. Box 16633 – 00620, Nairobi, Kenya.

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