Summary of Product Characteristics for Pharmaceutical Products

1. Name of the medicinal product
ACEAAR P

2. Qualitative and quantitative composition
Each film coated tablet contains Aceclofenac 100mg and Paracetamol 325mg.

For a full list of excipients, see section 6.1

3. Pharmaceutical form
Film-coated Tablet

Yellow coloured, oval shaped biconvex, film coated tablets

4. Clinical particulars

4.1 Therapeutic indications
Aceclofenac
Aceclofenac is indicated for the relief of pain and inflammation in osteoarthritis, rheumatoid arthritis and ankylosing spondylitis.

Paracetamol
For the treatment of mild to moderate pain including headache, migraine, neuralgia, toothache, sore throat, period pains,aches and pains, symptomatic relief of rheumatic aches and pains and of influenza, feverishness and feverish colds.

ACEAAR P 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.

4.2 Posology and method of administration
The recommended dose of ACEAAR P 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 Contraindications
Aceclofenac
Hypersensitivity to aceclofenac or to any of the excipients listed in section 6.1.

Active, or history of recurrent peptic ulcer/hemorrhage (two or more distinct episodes of proven ulceration or bleeding).
NSAIDs are contraindicated in patients who have previously shown hypersensitivity reactions (e.g. asthma, rhinitis, angioedema or urticaria)

in response to ibuprofen, aspirin, or other non- steroidal anti-inflammatory drugs.

Hepatic failure and renal failure.

Patient's with established congestive heart failure (NYHA IIIV), ischemic heart disease, peripheral arterial disease and/or cerebrovascular disease.

History of gastrointestinal bleeding or perforation, related to previous NSAIDs therapy.

Active bleeding's 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 (see section 4.6).

Paracetamol
Hypersensitivity to Paracetamol

4.4 Special warnings and precautions for use

Aceclofenac
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 or recovering from major surgery, and the elderly. The importance of prostaglandins in maintaining renal blood flow should be taken into account in these patients. Renal function should be monitored in these patients (see also section 4.3).

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. The lowest effective dose should be used and renal function monitored regularly. Effects on renal function are usually reversible on withdrawal of Aceclofenac.

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 should be discontinued. Close medical surveillance is necessary in patients suffering from mild to moderate impairment of hepatic function. Hepatitis may occur without prodromal symptoms.

Use of Aceclofenac in patients with hepatic porphyria may trigger an attack.

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.

Patients with congestive heart failure (NYHAI) and patients with significant risk factors for cardiovascular events (e.g. hypertension, hyperlipidemia, diabetes mellitus, smoking) should only be treated with aceclofenac after careful consideration. As the cardiovascular risks of aceclofenac may increase with dose and duration of exposure, the shortest duration possible and the lowest effective daily dose should be used. The patient's need for symptomatic relief and response to therapy should be reevaluated periodically. Aceclofenac should also be administered with caution and under close medical surveillance to patients with a history of cerebrovascular bleeding.

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. Close medical surveillance is imperative in patients with symptoms indicative of gastrointestinal disorders involving either the upper or lower gastrointestinal tract, with a history suggestive of gastro-intestinal ulceration, bleeding or perforation, wit ulcerative colitis or with Crohn's disease, or haematological abnormalities, as these conditions may be exacerbated (seesection 4.8)

The risk of GI bleeding, ulceration or perforation is higher with increasing NSAID doses, in patients with a history of ulcer, particularly if complicated with haemorrhage or perforation (see section 4.3), and in the elderly. These patients should commence treatment on the lowest dose available. Combination therapy with protective agents (e.g. misoprostol or proton pump inhibitors) should be considered for these patients, and also for patients requiring concomitant low dose aspirin, or other drugs likely to increase gastrointestinal risk (see below and section 4.5).

Patients with a history of GI toxicity, particularly when elderly, should report any unusual abdominal symptoms (especially GI bleeding) particularly in the initial stages of treatment. Caution should be advised in patients receiving concomitant medications which could increase the risk of ulceration or bleeding, such as systemic corticosteroids, anticoagulants such as warfarin, selective serotoninreuptake inhibitors or antiplatelet agents such as aspirin (see section 4.5).

When GI bleeding or ulceration occurs in patients receiving aceclofenac, the treatment should be withdrawn.

SLE and mixed connective tissue disease:

In patients with systemic lupus erythematosus (SLE) and mixed connective tissue disorders there may be an increased risk of aseptic meningitis (see section 4.8).

Dermatological:

Serious skin reactions, some of them fatal, including exfoliative dermatitis, StevensJohnson syndrome, and toxic epidermal necrolysis, have been reported very rarely in association with the use of NSAIDs (see section 4.8). Patients appear to be at highest risk for these reactions early in the course of therapy: the onset of the reaction occurring in the majority of cases within the first month of treatment. Aceclofenac should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity. Exceptionally, varicella

can trigger serious cutaneous and soft tissues infections complications. To date, the contributing role of NSAIDs in the worsening of these infections cannot be ruled out. Thus, it is advisable to avoid use of aceclofenac in case of varicella.

Hypersensitivity reactions:

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

Hematological
Aceclofenac may reversibly inhibit platelet aggregation (see section 4.5 anticoagulants under 'Interactions').

Long-term treatment:

All patients who are receiving NSAIDs should be monitored as a precautionary measure e.g. renal, hepatic function (elevation of liver enzymes may occur) and blood counts.

Paracetamol
Contains paracetamol. Do not use with any other paracetamol-containing products. Underlying liver disease increases the risk of paracetamol-related liver damage. Patients who have been diagnosed with liver or kidney impairment must seek medical advice before taking this medication.
Do not exceed the stated dose.
Patients should be advised to consult their doctor if their headaches become persistent. Patients should be advised to consult a doctor if they suffer from non-serious arthritis and need totake painkillers every day.
Caution should be exercised in patients with glutathione-depleted states, as the use of paracetamol may increase the risk of metabolic acidosis.
Use with caution in patients with glutathione depletion due to metabolic deficiencies

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, 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.

4.6 Fertility, pregnancy, and lactation

Aceclofenac

Pregnancy:

There is no information on the use of aceclofenac during pregnancy. Inhibition of prostaglandin synthesis may adversely affect the pregnancy and/or the embryo/fetal development. Data from epidemiological studies suggest an increased risk of miscarriage, cardiac malformation or gastroschisis after use of prostaglandin synthesis inhibitor in early pregnancy. The absolute risk for cardiovascular malformation was increased from less than 1%, up to approximately 1.5 %. The risk is believed to increase with dose and duration of therapy.

In animals, administration of a prostaglandin synthesis inhibitor has been shown to result in increased preimplantation loss and embryo-foetal lethality. In addition, increased incidences of various malformations, including cardiovascular, have been reported in animals given a prostaglandin synthesis inhibitor during the organogenetic period. During the first and second trimester of pregnancy, aceclofenac should not be given unless clearly.

If aceclofenac is used by a woman attempting to conceive, or during the first and second trimester of pregnancy, the dose should be kept as low and duration of treatment as short as possible.

During the third trimester of pregnancy, all prostaglandin synthesis inhibitors may expose the foetus to:

i. cardiopulmonary toxicity (with premature closure of the ductus arteriosus and pulmonary hypertension);

ii. renal dysfunction, which may progress to renal failure with oligo-hydroamniosis; the mother and the neonate, at the end of pregnancy, to:

iii. possible prolongation of bleeding time, an anti-aggregating effect which may occur even at very low doses.

iv. inhibition of uterine contractions resulting in delayed or prolonged labour. Consequently, aceclofenac is contraindicated during the third trimester of pregnancy (see section 4.3).

Lactation:

There is no information on the secretion of aceclofenac to breast milk; there was however no notable transfer of radio labelled (14C) aceclofenac to the milk of lactating rats..

The use of Aceclofenac should therefore be avoided in pregnancy and lactation unless the potential benefits to the other outweigh the possible risks to the foetus.

Paracetamol

Epidemiological studies in human pregnancy have shown no ill effects due to paracetamol used in the recommended dosage, but patients should follow the advice of the doctor regarding its use. Paracetamol is excreted in breast milk but not in a clinically significant amount. Available published data do not contraindicate breast feeding.

4.7 Effects on ability to drive and use machines.

Aceclofenac

Undesirable effects such as dizziness, drowsiness, vertigo, fatigue, visual disturbances or other central nervous system disorders are possible after taking NSAIDs. If affected, patients should not drive or operate machine.

Paracetamol

None known.

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.

Reporting of suspected adverse reactions: Healthcare professionals are asked to report any suspected adverse reactions via pharmacy and poisons board, Pharmacovigilance Electronic Reporting System (PvERS) https://pv.pharmacyboardkenya.org

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 Pharmacodynamic properties

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.

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' hydroxyaceclofenac. 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

There are no pre-clinical data of relevance to the prescriber which are additional to that already included in other sections of the SmPC.

6. Pharmaceutical particulars

6.1 List of excipients

Corn Starch
Diabasic Calcium Phosphate
Polyvidone (K-30)
Purified Water
Sodium starch Glycolate
Magnesium Stearate
Talc
Collodial Silicon Dioxide
Microcrystalline Cellulose
Instacoat (Yellow Oxide of Iron) (A10D00009)

6.2 Incompatibilities

None known

6.3 Shelf life

24 months

6.4 Special precautions for storage:

Store below 30˚C. Protect from light.

6.5 Nature and contents of container

PVC blister of 10 tablets. 3 such PVC blisters are packed in a printed carton along with the pack insert.

6.6 Special precautions for disposal and other handling:

Any unused product or waste material should be disposed of in accordance with local requirements.

7. Marketing authorization holder and manufacturing site addresses

Marketing authorization holder:

Pinnacle Life Science Pvt. Ltd.
Mahendra Industrial Estate,
Ground Floor Plot no .109-D, Rd no 29 Sion (East),
Mumbai 400 022, INDIA.

8. Marketing authorization number
H2022/CTD7223/14193

9. Date of first registration
02/09/2022

10. Date of revision of the text:
November 2024