Summary of Product Characteristics

1. NAME OF THE MEDICINAL PRODUCT

FECK (Aceclofenac Tablets 100 mg)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains:
Aceclofenac BP 100 mg

3 PHARMACEUTICAL FORM

Film-coated tablets
Light Orange colour, circular, slightly biconvex, film coated tablets, engraved with "ZIM" on one side and plain on other side.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Aceclofenac tablets is indicated for the treatment of inflammatory and painful processes such as low back pain, odontalgia, scapulohumeral periarthritis and extra-articular rheumatism, as well as for the chronic treatment of osteoarthritis, rheumatoid arthritis and ankylosing spondylitis.

4.2 Posology and method of administration

Adults
The recommended dose of aceclofenac is 200 mg daily, in two doses of 100 mg, one tablet in the morning and one in the evening.

Paediatric population
There are no clinical data on the use of this medicine in children

Elderly population
The pharmacokinetics of aceclofenac are not altered in elderly patients and therefore no dose or frequency of administration modification is considered necessary.
However, as with any other non-steroidal anti-inflammatory drug, precautions should be taken in the treatment of elderly patients, who are generally more prone to side effects, and who are more likely to have cardiovascular and renal or hepatic function disorders, as well as to receive concomitant medication.

Renal insufficiency
There is no evidence that the dosage of aceclofenac should be changed in patients with mild renal impairment (see section 4.4).

Hepatic impairment
Some evidence indicates that the dose of this medicinal product should be reduced in patients with hepatic impairment, suggesting the use of a dose of 100 mg *I* day.

Adverse reactions can be minimized by using the lowest effective dose during the shortest possible treatment period to control symptoms (see section 4.4 Special warnings and precautions for use).

Method of administration
Oral administration.
The tablets should be swallowed whole with a sufficient amount of liquid.
The contents of the sachets should be dissolved in about 40-60 ml of water and taken immediately.
When administering the drug to healthy volunteers, during meals or fasting, only the rate and not the degree of absorption of aceclofenac was altered, so Aceclofenac Tablets can be taken with food.

4.3 Contraindications

Hypersensitivity to aceclofenac or any of the excipients listed in section 6.1.

Aceclofenac must not be administered to patients with a history of gastrointestinal bleeding or perforation related to previous NSAID therapy, active or recurrent peptic ulcer/gastrointestinal bleeding (two or more different episodes of ulceration or bleeding proven).

It must also not be used in patients with active bleeding or bleeding disorders.

This medicine must not be used in patients with severe renal or hepatic impairment.

Aceclofenac Tablets must not be used in patients with established congestive heart failure (NYHA classification II-IV), ischaemic heart disease, peripheral arterial disease and/or cerebrovascular disease.

Aceclofenac should not be prescribed during the third trimester of gestation. During the first and second trimesters of pregnancy, Aceclofenac Tablets should not be administered unless strictly necessary. In this case, the dose and duration of treatment should be reduced as much as possible (see section 4.6).

Aceclofenac should not be prescribed during lactation (see section 4.6).

Aceclofenac Tablets must not be used in patients in whom aspirin or non-steroidal anti-inflammatory drugs trigger asthma attacks, acute rhinitis or urticarial, or in patients with hypersensitivity to these drugs.

4.4 Special warnings and precautions for use

Adverse reactions can be reduced if the lowest effective dose is used for the shortest possible time to control symptoms.

Concomitant administration of this medicinal product with other NSAIDs, including selective cyclo-oxygenase-2 (Coxib) inhibitors, should also be avoided.

Gastrointestinal risks:

Monitoring is required in patients with the following disorders as they may be aggravated (see section 4.8):

- Symptoms indicative of gastro-intestinal disorders affecting the upper or lower digestive tract.
- History suggestive of gastro-intestinal ulcer, bleeding, or perforation.
- IBcerative colitis
- Crohn's disease
- Haematological abnormalities

Gastrointestinal bleeding, ulcers and perforations: During treatment with nonsteroidal anti-inflammatory drugs (NSAIDs), including aceclofenac, gastrointestinal bleeding, ulcers and perforations (which may be fatal) have been reported at any time during treatment, with or without previous warning symptoms and with or without a prior history of serious gastrointestinal events.

The risk of gastrointestinal bleeding, ulcer or perforation is higher when increasing doses of NSAIDs are used, in patients with a history of ulcer, especially if they were ulcers complicated by bleeding or perforation (see section 4.3), and in elderly patients. These patients should start treatment at the lowest possible dose. It is recommended that these patients be prescribed concomitant treatment with protective agents (e.g. misoprostol or proton pump inhibitors); such combination therapy should also be considered for patients requiring low-dose aspirin or other medicinal products that may increase gastrointestinal risk (see below and section 4.5).
Patients with a history of gastrointestinal toxicity, and especially elderly patients, should be advised to report any unusual abdominal symptoms (especially gastrointestinal bleeding) to the physician immediately during treatment and particularly in the early stages.
Special caution should be advised for patients receiving concomitant therapies that could increase the risk of gastrointestinal ulcer or bleeding such as dicoumarin-type oral anticoagulants such as warfarin, and aspirin-type antiplatelet medicinal products (see section 4.5). Some caution should also be maintained in the concomitant administration of systemic corticosteroids and selective serotonin reuptake inhibitor (SSRI) antidepressants (see section 4.5).

If gastro-intestinal bleeding or ulcer occurs in patients receiving Aceclofenac Tablets, treatment should be discontinued immediately. Cardiovascular and cerebrovascular risks: Special caution should be exercised in patients with a history of hypertension and/or mild or moderate heart failure, as fluid retention and oedema have been reported in association with NSAID therapy.

Patients with congestive heart failure (NYHA-1) and patients with cardiovascular risk factors (e.g. hypertension, hyperlipidaemia, diabetes mellitus and smoking) should only be treated with aceclofenac after careful consideration. Since the cardiovascular risks of aceclofenac may increase with dose and duration of treatment, the lowest effective daily dose and the shortest possible duration of treatment should be used. The need for continued treatment and response should be reassessed periodically.

Aceclofenac should be administered with caution and under close medical supervision in patients with a history of cerebral hemorrhage.

Risk of severe skin reactions:
Serious, some fatal skin reactions, including exfoliative dermatitis, Stevens-Johnson syndrome and toxic epidermal necrolysis, have been reported with a very rare frequency, less than 1 case in 10,000 patients, in association with the use of NSAIDs (see section 4.8). It appears that patients are at increased risk of these reactions at the beginning of treatment: the occurrence of such an adverse reaction occurs in most cases during the first month of treatment. Airta1 should be discontinued immediately at the first symptoms of skin erythema, mucosal lesions or other signs of hypersensitivity.

Exceptionally, chickenpox can trigger serious skin complications and soft tissue infections. To date, the contribution of NSAIDs to the aggravation of these infections cannot be ruled out. For this reason, it is recommended to avoid the use of aceclofenac in case of chickenpox.

Risk of allergic reactions:
As with any other non-steroidal anti-inflammatory drug, allergic reactions, including anaphylactic/anaphylactoid reactions, may occur without prior exposure to the drug (see section 4.8).

Elderly patients:
Elderly patients experience an increased incidence of adverse reactions to NSAIDs, specifically gastrointestinal bleeding and perforation, which may be fatal (see section 4.2).

Patients with renal impairment:
Administration of an NSAID may result in a dose-dependent reduction in prostaglandin formation and lead to renal failure. The importance of prostaglandins in maintaining renal blood flow should be taken into account in patients with heart or kidney failure, hepatic impairment, patients on diuretic therapy or recovering from major surgery, and in elderly patients. Patients with mild or moderate renal impairment should be monitored as the use of NSAIDs may lead to deterioration of renal function. It is advisable to administer the lowest effective dose and regular monitoring of renal function. The effects on renal function are reversed with discontinuation of treatment with Aceclofenac Tablets.

Patients with Hepatic impairment:
Patients with mild or moderate hepatic impairment should be adequately monitored for laboratory parameters of hepatic function and initiate treatment with 100 mg once daily (see section 4.2).
In any patient (with or without previous impairment of hepatic function), administration of Airta1 should be discontinued if hepatic function controls worsen or do not normalize and if symptoms or other manifestations (e.g. eosinophilia, rash) suggestive of liver disease occur. Hepatitis may occur without prodromal symptoms

(see section 4.8), so quarterly monitoring of liver function is recommended for long-term therapy.
Administration of this medicine in patients with hepatic porphyria may trigger an attack.

Hematological risks:
Aceclofenac may reversibly inhibit platelet aggregation (see section 4.5).

Respiratory Disorder:
It should be used with caution in patients with or with a history of bronchial asthma, as NSAIDs have been reported to trigger bronchospasm in these patients.

Other warning:

Caution should be exercised when aceleclofenac is administered concomitantly with the following medicinal products: lithium, digoxin, anticoagulants, oral antidiabetics, other anti-inflammatory drugs, as it may increase the frequency of adverse reactions or it may be necessary to adjust the dose of Aceclofenac or these medicinal products.

Long-term treatment:

As a precautionary measure, all patients receiving long-term treatment with nonsteroidal anti-inflammatory agents (e.g., kidney, liver, and blood count) should be followed up.

Excipient warnings

Aceclofenac Tablets 100 mg powder for oral suspension·

This medicine contains 2,639 mg of sorbitol in each sachet. Patients with hereditary fructose intolerance (FHI) should not take this medicine.

This medicine contains 10 mg of aspartame in each sachet. Aspartame contains a source of phenylalanine that can be harmful if you have phenylketonuria (PKF).

Aceclofenac powder/tablets, contain less than 23 mg sodium (1 mmol) per sachet/tablet; that is, essentially "sodium-free."

4.5 Interaction with other medicinal products and other forms of interaction

Lithium and digoxin: Many nonsteroidal anti-inflammatory drugs inhibit renal clearance of lithium and digoxin, increasing serum concentrations of both. Combination therapy should be avoided unless frequent monitoring of lithium and digoxin levels can be performed (see section 4.4).

Diuretics: Animal studies indicate the possibility that aceclofenac, like other nonsteroidal anti-inflammatory drugs, may interfere with the natriuretic action of diuretics. This property may have clinical significance in hypertensive patients or patients with compromised cardiac function.

No effect of aceclofenac on blood pressure control was observed when co-administered with bendrofluazide, although interaction with other diuretic drugs cannot be excluded.

When administered concomitantly with potassium-sparing diuretics, serum potassium levels should be monitored.

Antihypertensives: NSAIDs may reduce the effect of antihypertensives. The risk of acute renal failure, which is normally reversible, may be increased in some patients with compromised renal function (e.g. dehydrated patients or elderly patients) when ACE inhibitors or angiotensin II receptor antagonists are combined with nonsteroidal anti- inflammatory drugs. For this reason, concomitant administration should be undertaken with caution especially in elderly patients. Patients should be adequately hydrated and monitoring of renal function should be considered after initiation of concomitant therapy, which should be performed periodically thereafter.

Anticoagulants: Like other nonsteroidal anti-inflammatory agents, aceclofenac may increase the effects of dicoumarin- type anticoagulants due to a possible action of inhibiting platelet aggregation. Patients receiving combination therapy with anticoagulants and Aceclofenac Tablets should be adequately monitored (see section 4.4).

Antiplatelet agents: Antiplatelet agents increase the risk of gastrointestinal bleeding (see section 4.4).

Oral antidiabetics: Clinical studies have shown that aceclofenac can be administered concomitantly with oral antidiabetics without altering their clinical effect. However, isolated cases of hypoglycaemia and hyperglycaemia have been reported. Consideration should be given to adjusting the dose of hypoglycaemic agents when Aceclofenac Tablets is administered (see section 4.4).

Methotrexate: The possible interaction between nonsteroidal anti-inflammatory drugs and methotrexate should be taken into account when using low doses of methotrexate, especially in patients with renal impairment. In case of combination therapy, renal function should be monitored. Caution should be taken if non-steroidal anti-inflammatory drugs and methotrexate are administered less than 24 hours apart, because nonsteroidal anti-inflammatory drugs may increase methotrexate plasma concentrations, leading to increased toxicity.

Corticosteroids: Corticosteroids may also increase the risk of gastrointestinal ulcer or bleeding (see section 4.4).

Concomitant treatment with aspirin and other non-steroidal anti-inflammatory drugs may increase the frequency of side effects (see section 4.4).

SSRIs: Selective serotonin reuptake inhibitors (SSRIs) may also increase the risk of gastrointestinal bleeding (see section 4.4).

Cyclosporine, tacrolimus: Concomitant administration of nonsteroidal anti-inflammatory drugs and cyclosporine or tacrolimus is thought to increase the risk of nephrotoxicity due to reduced synthesis of prostacyclin in the kidney. For this reason, close monitoring of kidney function during combination therapy is important.

Zidovudine: Co-administration of zidovudine and NSAIDs may increase the risk of haematological toxicity. There is evidence of increased risk of haemoarthrosis and haematomas in HIV (+) haemophiliacs receiving co-treatment with zidovudine and ibuprofen.

4.6 Fertility, pregnancy and lactation

4.6.1. Pregnancy

There is no information regarding the use of aceclofenac during pregnancy.

1) First and second trimester of gestation

Inhibition of prostaglandin synthesis may adversely affect pregnancy and/or embryo/foetus development. Data from epidemiological studies suggest an increased risk of miscarriage and cardiac malformations and gastroschisis following the use of a prostaglandin synthesis inhibitor early in gestation. The absolute risk of cardiac malformations increased from less than 1% to approximately 1.5%. It appears that the risk increases with dose and duration of treatment.

In animals, administration of a prostaglandin synthesis inhibitor showed greater pre- and post-implantation loss and higher embryo/foetus mortality. An increased incidence of several malformations, e.g. cardiovascular, was also reported in animals administered a prostaglandin synthesis inhibitor during the organogenetic period. From the 20th week of pregnancy, the use of aceclofenac may cause oligohydramnios as a result of foetal renal dysfunction. This can occur soon after the start of treatment and is usually reversible when stopped. In addition, there have been reports of constriction of the ductus arteriosus after treatment in the second trimester, most of which resolved after cessation of treatment.

Therefore, during the first and second trimesters of gestation, aceclofenac should not be administered unless it is clearly considered necessary. If aceclofenac is used by a woman trying to become pregnant, or during the first and second trimesters of pregnancy, the dose and duration of treatment should be reduced as much as possible. Prenatal monitoring for oligohydramnios and ductus arteriosus constriction should be considered after exposure to aceclofenac for several days from gestational week 20 onwards. Aceclofenac should be discontinued if oligohydramnios constriction or ductus arteriosus is found.

2) Third trimester of gestation

During the third trimester of gestation, all prostaglandin synthesis inhibitors can expose the fetus to:

- Cardiopulmonary toxicity (constriction/premature closure of the ductus arteriosus and pulmonary hypertension)
- Renal dysfunction (see above). And to the mother and newborn, at the end of gestation,
- Possible prolongation of bleeding time, due to an antiplatelet effect that can occur even at very low doses.
- Inhibition of uterine contractions, which can delay or prolong labor.

Consequently, aceclofenac is contraindicated during the third trimester of pregnancy (see sections 4.3 and 5.3).

4.6.2. Breastfeeding

Aceclofenac Tablets should not be administered during lactation. No information is available on its secretion in breast milk; however, no notable transfer of labeled aceclofenac (l4C) to rat milk was observed during lactation.

Therefore, the use of aceclofenac during pregnancy and lactation should be avoided except in cases where the potential benefits to the mother outweigh the possible risks to the fetus.

4.6.3. Fertility

The use of aceclofenac may alter female fertility and is not recommended in women who are trying to conceive. In women who have difficulty conceiving or who are undergoing fertility research, discontinuation of this medication should be considered.

4.7 Effects on ability to drive and use machines

Patients with signs or symptoms of central nervous system disorders such as dizziness, dizziness or fainting should not drive or use machinery while being treated with nonsteroidal anti-inflammatory drugs.

4.8 Undesirable effects

The most frequently observed adverse reactions are gastrointestinal in nature. Peptic ulcers, perforation or gastrointestinal bleeding may occur, in some cases fatal, especially in the elderly (see section 4.4). Nausea, vomiting, diarrhoea, flatulence, constipation, dyspepsia, abdominal pain, melena, hematemesis, ulcerative stomatitis, exacerbation of colitis and Crohn's disease have also been reported (see section 4.4). The occurrence of gastritis has been observed less frequently.
Exceptionally, serious skin complications and soft tissue infections have been reported during chickenpox in association with treatment with nonsteroidal anti-inflammatory drugs.

Aceclofenac is metabolized to diclofenac and is structurally close to diclofenac. Associated with the use of diclofenac, there is a large amount of clinical and epidemiological data that consistently indicate an increased risk of arterial thrombotic events (myocardial infarction or stroke, particularly at high doses and in long-term treatments).
Epidemiological data also show an increased risk of acute coronary syndrome and myocardial infarction associated with the use of aceclofenac (see sections 4.3 and 4.4 on Contraindications and Special warnings and precautions for use).

If serious adverse reactions occur, administration of Aceclofenac Tablets should be discontinued.
During all clinical trials, and subsequently corroborated by post-marketing experience, the following adverse effects have been observed, which are classified by system organs

and frequencies. Frequencies are defined as: very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥ 1/1000 to <1/100); (≥1/10,000 to <1/1,000) or very rare (<1/10,000).

MedDRa Organic Systems	**Frequent (≥1/100 to <1/10)**	**Uncommon (≥ 1/1000 to <1/100)**	**Rare (≥1/10,000 to <1/1,000)**	**Very rare (<1/10,000)**
Blood and lymphatic system disorders			Anaemia	Bone marrow depression Granulocytopenia Thrombocyto
Immune system disorders			Anaphylactic reaction (including shock) Hypersensitivity	
Metabolism and nutrition				Hyperkalemia
Psychiatric disorders				Depression Sleep disorder
Nervous system disorders	Dizziness			Paresthesia Sleepiness Headache Dysgeusia (taste disorder)
Eye disorders			Visual impairment	
Ear and labyrinth disorders				Vertigo Tinnitus
Cardiac disorders			Heart failure	Palpitations
Vascular disorders			High blood pressure	Rubefaction Heat Peripheral edema

See sections 4.4 and 4.5 for more information on warnings, precautions and interactions.

Reporting of suspected adverse reactions
It is important to report suspected adverse reactions to the medicinal product after authorization. This allows continuous monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are invited to report suspected adverse reactions through website www.zimlab.com

4.9 Overdose
Treatment of acute poisoning by nonsteroidal anti-inflammatory drugs consists essentially of supportive and symptomatic measures for complications such as hypotension, renal failure, seizures, gastrointestinal irritation and respiratory depression.

No data are available on the consequences of Aceclofenac Tablets overdose in humans. The therapeutic measures to be adopted are: after overdose, absorption of the drug should be avoided as soon as possible by gastric lavage and treatment with activated charcoal.

Specific treatments such as forced diuresis, dialysis or haemoperfusion are unlikely to help eliminate non-steroidal anti-inflammatory drugs because of their high protein binding rate and high metabolism.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Non-steroidal anti-inflammatory and antirheumatic products. Acetic acid derivatives and related substances.
(ATC code: M01AB16).

Aceclofenac is a non-steroidal agent with remarkable anti-inflammatory and analgesic properties.

The mode of action of aceclofenac is largely based on inhibition of prostaglandin synthesis. Aceclofenac is a potent inhibitor of the enzyme cyclo-oxygenase, which is involved in the production of prostaglandins.

5.2 Pharmacokinetic properties
Following oral administration, aceclofenac is rapidly and completely absorbed as unchanged drug. Peak plasma concentrations are reached approximately 1.25 to 3.00 hours after ingestion. Aceclofenac penetrates the synovial fluid, where its concentrations reach approximately 57% of those of plasma. The volume of distribution is approximately 25 I.
The plasma half-life is about 4 hours. Aceclofenac is largely protein bound (> 99%). Aceclofenac circulates primarily in unchanged drug form. The major metabolite detected in plasma is 4'-hydroxyaceclofenac. Approximately two thirds of the administered dose is excreted in the urine, mainly in the form of hydroxymetabolites.

No alterations in the pharmacokinetics of aceclofenac have been detected in elderly patients.

5.3 Preclinical safety data

The results of preclinical studies with aceclofenac are consistent with those expected for nonsteroidal anti-inflammatory drugs. The main target organ was the gastrointestinal tract. No unexpected findings were recorded.

Aceclofenac was not considered to have any mutagenic activity in three in *vitro* studies and in *one in vivo* mouse study. However, in a study with rabbits, treatment with aceclofenac (10 mg/kg/day) caused a number of morphological alterations in some fetuses.

Teratogenesis studies in rats were negative and did not show any abnormalities. Aceclofenac was not found to be carcinogenic in either the mouse or rat.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet Core:
Maize Starch
Lactose
Microcrystalline cellulose
Methyl hydroxyl benzoate
Propyl hydroxyl benzoate
Colloidal anhydrous silica
Magnesium stearate
Sodium starch glycolate
Purified talc

Tablet Coat:
Opadry Orange

6.2 Incompatibilities

Not applicable

6.3 Shelf-life

36 Months

6.4 Special precautions for storage

Store at temperature not exceeding 30º C, Protect from light and moisture.

6.5 Nature and content of container

Alu-PVC blister pack of 10 x 10 tablets

6.6 Special precautions for disposal

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

7. MARKETING AUTHORISATION HOLDER

Zim Laboratories Limited.
Sadoday Gyan (Ground Floor),
Opp. NADT, Nelson Square,
Nagpur – 440013
India.

8. MARKETING AUTHORISATION NUMBERS

04544/5965/NMR/2018

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

02/07/2019

10. DATE OF REVISION OF THE TEXT

01/07/2023