1.6 Product Information

1.6.1 Prescribing Information (Summary of Product Characteristics)

1. Name of the Medicinal Product

1.1 Trade Name **:** FECK (Aceclofenac Tablets 100 mg)

1.2 Strength **:** 100 mg

1.3 Pharmaceutical Form **:** Film Coated Tablets

2. Qualitative and Quantitative Composition

S. No	**Name of Ingredients**	**Quantity/ Tablets (mg)**
Active Substance		
1	Aceclofenac	100.00
Inactive Substance		
2	Maize Starch	110.00
3	Lactose Monohydrate	47.90
4	Microcrystalline Cellulose	50.00
5	Methyl Hydroxybenzoate	0.50
6	Propyl Hydroxybenzoate	0.10
7	Colloidal Anhydrous Silica	1.00
8	Magnesium Stearate	4.00
9	Sodium Starch Glycolate	15.00
10	Purified Talc	6.50
11	Opadry Orange	10.00
12	Purified Water	Q.S.
	Total	**345.00 mg**

3. Pharmaceutical Form

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

4. Clinical Particulars

4.1 Therapeutic indications

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

4.2 Posology and method of administration

Posology

Adults: The maximum recommended dose is 200 mg daily, taken as two separate doses of 100 mg, one tablet in the morning and one tablet in the evening.
Children: There are no clinical data supporting the use of aceclofenac in children therefore its use is not recommended.
Elderly: Caution should be exercised in the treatment of elderly patients, who are generally more prone to adverse reactions, and who are more likely to be suffering from impaired renal, cardiovascular or hepatic function and receiving concomitant medication. If an NSAID is considered necessary, the lowest effective dose should be used and for the shortest possible duration. The elderly should be monitored for GI bleeding regularly during NSAID therapy. The pharmacokinetics of aceclofenac are not altered in elderly patients, therefore it is not considered necessary to modify the dose or dose frequency.
Renal insufficiency: There is no evidence to suggest that the dosage needs to be altered for patients with mild renal impairment, however caution should be exercised.
Hepatic insufficiency: There is some evidence that the dose of aceclofenac should be reduced in patients with hepatic impairment. It is suggested that an initial daily dose of 100 mg is used. Undesirable effects may be minimized by using the lowest effective dose for the shortest duration necessary to control symptoms.

Method of administration

For oral use. Aceclofenac Tablets should be swallowed whole with liquid.
Aceclofenac may be taken with or after food.

4.3 Contraindication

This medicinal product is contraindicated in the following situations:

- Hypersensitivity to the active substance or to any of the excipients in this formulation.
- Patients with history of gastrointestinal bleeding or perforation, related to previous NSAIDs therapy
- Active or history of recurrent peptic ulcer/haemorrhage (two or more distinct episodes of proven ulceration or bleeding).
- Patients with active bleedings or bleeding disorders.

- Patients with hepatic failure and renal failure.
- Patients with established congestive heart failure (NYHA class II-IV), ischaemic heart disease, peripheral arterial disease and/or cerebrovascular disease.
- Patients in whom acetylsalicylic acid or NSAIDs precipitate attacks of asthma, acute rhinitis, angioedema or urticaria or who are hypersensitive to these drugs
- Third trimester of pregnancy.

4.4 Special warnings and special precautions for use

The use of aceclofenac with other concomitant NSAIDs including cyclooxygenase-2-selective inhibitors should be avoided.

Undesirable effects may be minimized by using the lowest effective dose for the shortest duration necessary to control symptoms.

Elderly: The elderly have an increased frequency of adverse reactions to NSAIDs especially gastrointestinal bleeding and perforation which may be fatal.

Gastrointestinal: Close medical surveillance is needed in patients with the following conditions as these may be exacerbated:

- Symptoms indicative of gastrointestinal disease involving either the upper or lower gastrointestinal tract
- A history suggestive of gastrointestinal ulceration, bleeding or perforation
- Ulcerative colitis
- Crohn's disease
- Haematological abnormalities

GI bleeding, ulceration or perforation, which can be fatal, have been reported with all NSAIDs at any time during treatment, with or without warning symptoms or a previous history of serious GI events.

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 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.

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 serotonin-reuptake inhibitors or anti-platelet agents such as aspirin.

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.

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

Patients appear to be at highest risk of 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.

Cardiovascular and cerebrovascular: 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 (NYHA-I), and patients with significant risk factors for cardiovascular events (e.g. hypertension, hyperlipidaemia, 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 re-evaluated periodically. Aceclofenac should also be administered with caution and under close medical surveillance to patients with a history of cerebrovascular bleeding.

Cardiovascular, renal and hepatic impairment: The administration of an NSAID may cause a dose dependent reduction in prostaglandin formation and precipitate renal failure. The importance of prostaglandins in maintaining renal blood flow should be taken into account in patients with impaired cardiac or renal function, liver dysfunction, those being treated with diuretics or recovering from major surgery and the elderly. Renal function should be monitored in these patients

Renal: Patients with mild to moderate renal or cardiac impairment and the elderly 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: Close medical surveillance is needed in patients suffering from mild to moderate hepatic function impairment. Aceclofenac should be discontinued if abnormal liver function tests persist or worsen, clinical signs or symptoms consistent with liver disease develop or if other manifestations occur (eosinophilia, rash). Hepatitis may occur without prodromal symptoms. Use of NSAIDs in patients with hepatic porphyria may trigger an attack.

Hematological: Aceclofenac may reversibly inhibit platelet aggregation.

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.
Long-term treatment: All patients who are receiving long-term treatment with NSAIDs should be monitored as a precautionary measure (*e.g.* renal, hepatic function (elevation of liver enzymes may occur) and blood counts).

4.5 Interaction with other medicinal products and other forms of interaction
Lithium: It inhibit the renal clearance of lithium, resulting in increased serum concentrations of lithium. The combination should be avoided unless frequent monitoring of lithium can be performed.
Cardiac glycosides: NSAIDs may exacerbate cardiac failure, reduce the GFR (glomerular filtration rate) and inhibit the renal clearance of glycosides, resulting in increased plasma glycoside levels. The combination should be avoided unless frequent monitoring of glycosides can be performed.
Diuretics: Aceclofenac, like other NSAIDs, may inhibit the activity of diuretics. Although it was not shown to affect blood pressure control when co-administered with bendroflumethiazide, interactions with other diuretics cannot be ruled out. When concomitant administration with potassium-sparing diuretics is employed, serum potassium should be monitored. Diuretics can increase the risk of nephrotoxicity of NSAIDs.
Antihypertensive: NSAIDs may reduce the effect of antihypertensive. The risk of acute renal insufficiency, which is usually 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 NSAIDs. Therefore, the combination should be administered with caution, especially in the elderly. Patients should be adequately hydrated and consideration should be given to monitoring of renal function after initiation of concomitant therapy, and periodically thereafter.
Anticoagulants: Like other NSAIDs, aceclofenac may enhance the activity of anticoagulants such as warfarin. Close monitoring of patients on combined anticoagulant and Aceclofenac therapy should be undertaken.
Antidiabetic agents: Clinical studies have shown that diclofenac can be given together with oral antidiabetic agents without influencing their clinical effect. However, there have been isolated reports of hypoglycaemic and hyperglycemic effects. Thus with aceclofenac, consideration should be given to adjustment of the dosage of hypoglycaemic agents.
Methotrexate: Caution should be exercised if NSAID and methotrexate are administered within a 24-hour period, since the methotrexate levels may increase and result in increased toxicity.
Mifepristone: NSAIDs should not be used for 8-12 days after mifepristone administration as NSAIDs can reduce the effect of mifepristone.
Other NSAIDs: Concomitant therapy with acetylsalicylic acid and other NSAIDs, including cyclo-oxygenase-2 selective inhibitors, should be avoided as they may increase the frequency of side effects, including GI bleeding.

Corticosteroids: increased risk of gastrointestinal ulceration or bleeding.
Anti-platelet agents and selective serotonin reuptake inhibitors (SSRIs): combined with NSAIDs may increase the 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.
Quinolone antimicrobials: Convulsions may occur due to an interaction between quinolones and NSAIDs. Therefore, caution should be exercised when considering the use of a quinolone in patients who are already receiving a NSAID.
Zidovudine: When NSAIDs are given with zidovudine there is an increased risk of haematological toxicity. There are indications of an increased risk of haemoarthroses and haematoma in HIV(+) haemophiliacs receiving concurrent treatment with zidovudine and ibuprofen.

4.6 Pregnancy and lactation
Pregnancy: There is no information on the use of aceclofenac during pregnancy. Aceclofenac is contraindicated during the third trimester of pregnancy
Lactation: The use of aceclofenac should therefore be avoided in lactation unless the potential benefits to the mother outweigh the possible risks to the foetus.
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 investigations for infertility, withdrawal of aceclofenac should be considered.

4.7 Effects on ability to drive and use machines
Patients suffering from dizziness, drowsiness, vertigo, fatigue, visual disturbances or other central nervous system disorders whilst taking NSAIDs should refrain from driving or handling dangerous machinery.

4.8 Undesirable effects
Gastrointestinal: The most commonly observed adverse events 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 (a) non-specific allergic reactions and anaphylaxis (b) respiratory tract reactivity comprising asthma, aggravated asthma, bronchospasm or dyspnoea, or (c) 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 and cerebrovascular: Oedema, hypertension and cardiac failure have been reported in association with NSAID treatment.
Exceptionally, occurrence of serious cutaneous and soft tissues infections complications during varicella has been reported in association with NSAID treatment.
Aceclofenac is both structurally related and metabolised to diclofenac for which a greater amount of clinical and epidemiological data consistently point towards an increased risk of general arterial thrombotic events (myocardial infarction or stroke, particularly at high doses and in long treatment). Epidemiological data has also found an increased risk of acute coronary syndrome and myocardial infarction associated with the use of aceclofenac.
Other adverse reactions reported less commonly include:
Renal: Interstitial nephritis
Neurological and special senses: Optic neuritis, reports of aseptic meningitis (especially in patients with existing auto immune disorders, such as systemic lupus erythematosus, mixed connective tissue disease), with symptoms such as stiff neck, headache, nausea, vomiting, fever or disorientation (see section 4.4), confusion, hallucinations, malaise and drowsiness.
Haematological: Agranulocytosis, aplastic anaemia
Dermatological: Bullous reactions including Stevens-Johnson syndrome and toxic epidermal necrolysis (very rare), erythema multiforme, exfoliative dermatitis, photosensitivity.
If serious adverse reactions occur, aceclofenac should be withdrawn.
The following adverse reaction observed while taking Aceclofenac. The frequency grouping is defined using the following convention: Common (≥1/100 to <1/10); Uncommon (≥1/1,000 to <1/100); Rare (≥1/10,000 to <1/1,000); Very rare (<1/10,000)
Common: Dizziness, Dyspepsia, Abdominal pain, Nausea, Diarrhoea, Hepatic enzyme increased.
Uncommon: Flatulence, Gastritis, Constipation, Vomiting, Mouth ulceration, Pruritus, Rash, Dermatitis, Urticaria, Blood urea increased, Blood creatinine increased.
Rare: Anaemia, Anaphylactic reaction (including shock), Hypersensitivity, Visual disturbance, Cardiac failure, Hypertension, Dyspnoea, Melaena, Gastrointestinal haemorrhage, Gastrointestinal ulceration, Angioedema.
Very rare: Bone marrow depression, Granulocytopenia, Thrombocytopenia, Neutropenia, Haemolytic anaemia, Hyperkalaemia, Depression, Abnormal dreams, Insomnia, Paraesthesia, Tremor, Somnolence, Headache, Dysgeusia (abnormal taste), Vertigo, Tinnitus, Palpitations, Flushing, Hot flush, Vasculitis, Bronchospasm, Stridor, Stomatitis, Haematemesis, Intestinal perforation, Exacerbation of Crohn's disease and Colitis Ulcerative, Pancreatitis, Hepatic injury (including hepatitis), Jaundice, Purpura, Dermatitis bullous, Severe mucocutaneous skin reaction (including Stevens Johnson Syndrome and Toxic Epidermal Necrolysis), Renal failure, Nephrotic syndrome, Oedema, Fatigue, Cramps in legs, Weight increase, Blood alkaline phosphatase increased.

4.9 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 and convulsions. In cases of significant poisoning acute renal failure and liver damage are possible.

Management: 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.

Specific therapies such as dialysis or haemoperfusion are probable of no help in eliminating NSAIDs due to their high rate of protein binding and extensive metabolism.

Good urine output should be ensured. Renal and liver function should be closely monitored.

Patients should be observed for at least four hours after ingestion of potentially toxic amounts.

In case of frequent or prolonged convulsions, patients should be treated with intravenous diazepam.

Other measures may be indicated by the patient's clinical condition.

Management of acute poisoning with oral aceclofenac essentially consists of supportive and symptomatic measures for complications such as hypotension, renal failure, convulsions, gastrointestinal irritation, and respiratory depression.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamics properties

Pharmacotherapeutic group : Anti-inflammatory and Antirheumatics products, non-steroids, acetic acid derivatives and related substances.

ATC code : M01AB16.

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

5.2 Pharmacokinetic Properties

Absorption: After oral administration, Aceclofenac is rapidly and completely absorbed as unchanged drug. Peak plasma concentrations are reached approximately 1.25 to 3.00 hours following ingestion.

Distribution: Aceclofenac penetrates into the synovial fluid, where the concentrations reach approximately 57% of those in plasma. The volume of distribution is approximately 25 L. The mean plasma elimination half-life is around 4 hours. Aceclofenac is highly protein-bound (> 99%).

Biotransformation and elimination: Aceclofenac circulates mainly as unchanged drug. 4'-Hydroxyaceclofenac is the main metabolite detected in plasma. Approximately two-thirds of the administered dose is excreted via the urine, mainly as hydroxymetabolites.

Elderly: No changes in the pharmacokinetics of aceclofenac have been detected in the elderly.

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.
Animal studies indicate that there was no evidence of teratogenesis in rats although the systemic exposure was low and in rabbits, treatment with aceclofenac (10 mg/kg/day) resulted in a series of morphological changes in some fetuses.

6. Pharmaceutical Particulars

6.1 List of excipients

Maize Starch
Lactose Monohydrate
Microcrystalline cellulose
Methyl Hydroxybenzoate
Propyl Hydroxybenzoate
Colloidal anhydrous silica
Magnesium Stearate
Sodium Starch Glycolate (Type A)
Purified Talc
Opadry Orange

6.2 Incompatibilities

None

6.3 Shelf life

3 years from the date of manufacture

6.4 Special precautions for storage

Store at temperature not exceeding 30°C, protect from light and moisture.

6.5 Nature and contents of container

3 x 10 Film coated tablets packed in Alu-Alu Blister Pack.

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

ZIM Laboratories Limited
B-21/22, MIDC Area,

Kalmeshwar, Nagpur 441501
Maharashtra State,
India.

8. Number(S) In the National Register of Finished pharmaceutical products
NA

9. Date of First Authorization/Renewal of the Authorization
NA

10. Date of Revision of the Text
0 June 2019