Summary of Product Characteristics for Pharmaceutical Products

1. Name of the medicinal product:

ACLOSARA® MR

Aceclofenac, Paracetamol & Chlorzoxazone Tablets.

2. Qualitative and quantitative composition

Each film coated tablet contains:

Aceclofenac BP	100 mg
Paracetamol BP	325 mg
Chlorzoxazone USP	250 mg
Excipients	q.s.

Colour: Sunset Yellow & Titanium Dioxide BP

(for the full list of excipients, see section 6.1)

3. Pharmaceutical form:

Film coated tablet

Orange coloured, elongated shaped, biconvex film coated tablets, one side break line and other side plain.

4. Clinical particulars

4.1 Therapeutic indications

ACLOSARA® MR is indicated for the relief of pain & inflammation in osteoarthritis, painful musculoskeletal disorders with associated skeletal muscle spasm, rheumatoid arthritis and ankylosing spondylitis.

4.2 Posology and method of administration

ACLOSARA® MR tablets are supplied for oral administration and should be swallowed whole with a suffcient quantity of liquid. It should be taken preferably with or after food 1-2 times a day or as directed by physician.

ACLOSARA® MR tablets are not recommended for use in children.

Method of administration

For Oral use.

4.3 Contraindications

- Known hypersensitivity to aceclofenac or to paracetamol or to chlorzoxazone or to any component of the formulation.
- Active or history of recurrent peptic ulcer, bleeding or bleeding disorders.
- History of gastrointestinal (GI) bleeding or perforation, relating to previous NSAID therapy.
- Severe heart failure, hepatic failure and renal failure.
- Patients with established congestive heart failure (NYHA class II-IV), ischemic heart disease, peripheral arterial disease and/or cerebrovascular disease.
- During pregnancy & lactation.

- Patients in whom attacks of asthma, urticaria, or acute rhinitis are precipitated by aspirin or other NSAIDs.
- Known intolerance to chlorzoxazone.
- Porphyria, liver disease.

4.4 Special warnings and precautions for use

Close medical surveillance is imperative in patients with symptoms indicative of gastro-intestinal disorders, with a history suggestive of gastro-intestinal ulceration, with ulcerative colitis or with Crohn's disease, bleeding diathesis or haematological abnormalities.

Gastro-intestinal bleeding or ulcerative perforation, haematemesis and melaena have in general more serious consequences in the elderly. They can occur at any time during treatment, with or without warning symptoms or a previous history. In the rare instances where gastro-intestinal bleeding or ulceration occurs in patients receiving Aceclofenac, the drug should be withdrawn.

Close medical surveillance is also imperative in patients suffering from severe impairment of hepatic function.

4.5 Interaction with other medicinal products and other forms of interaction.

Aceclofenac

Like many NSAIDs, aceclofenac may increase plasma concentrations of lithium. Through their renal effects, NSAIDs may increase plasma glycoside (including digoxin) levels, exacerbate cardiac failure and reduce the glomerular filtration rate in patients receiving glycosides.

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 bendrofluazide, 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.

Quinolone Antimicrobials: Convulsions may occur due to an interaction between quinolones and NSAIDs. This may occur in patients with or without a previous history of epilepsy or convulsions. Therefore, caution should be exercised when considering the use of a quinolone in patients who are already receiving a NSAID.

Paracetamol

Cholestyramine: The rate of absorption of paracetamol is reduced by cholestyramine. Therefore, cholestyramine should not be taken within one hour, if maximal analgesia is required.

Metoclopramide and Domperidone: The absorption of paracetamol is increased by metoclopramide and domperidone. However, concurrent use need not be avoided.

Warfarin: The anti-coagulant effect of warfarin and other coumarins may be enhanced by prolonged regular use of paracetamol with increased risk of bleeding; occasional doses have no significant effect.

Chloramphenicol: Concurrent administration of paracetamol and chloramphenicol may markedly retard the elimination of chloramphenicol and thus, increases plasma concentration of chloramphenicol which leads to risk of its harmful effects. Monitoring of chloramphenicol plasma levels is recommended while combining paracetamol with chloramphenicol injection. Alcohol, Anticonvulsants, and Isoniazid: Concomitant administration of alcohol, anticonvulsants, and isoniazid with paracetamol may increase risk of hepatotoxicity.

Chlorzoxazone
CNS Depressants: Patients receiving antipsychotics, antianxiety agents or other CNS depressants concomitantly with this drug may exhibit an additive CNS depression. When such combined therapy is contemplated, the dose of one or both agents should be reduced.
Alcohol: Concomitant use of alcohol with chlorzoxazone will exacerbate the CNS depression and should be avoided. Patients suffering from alcoholism or currently under ethanol intoxication should not use chlorzoxazone. Codeine/Dihydrocodeine/Hydrocodone: Concomitant use of opiate agonists with skeletal muscle relaxants may cause respiratory depression, hypotension, profound sedation, and death. Limit the use of opioid pain medications with skeletal muscle relaxants to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect.

4.6 Fertility, pregnancy and lactation
No well controlled studies are available regarding the use of Aceclofenac with Paracetamol & chlorzoxazone in pregnancy and lactation. Thus use ACLOSARA® MR is not recommended for use in pregnancy and nursing mothers.

4.7 Effects on ability to drive and use machines
Undesirable effects such as dizziness, drowsiness, fatigue, and visual disturbances are possible after taking NSAIDs, including aceclofenac. Further, CNS depressant effects of chlorzoxazone may impair driving or operating machinery or the ability to perform other hazardous activities. Thus, patients are advised not to drive vehicles or operate machinery while taking this medicine.

4.8 Undesirable effects
The majority of adverse reactions reported have been reversible and of a minor nature. The most frequent are gastrointestinal disorders, in particular dyspepsia, abdominal pain, nausea and diarrhoea, and occasional occurrence of dizziness. Dermatological complaints including pruritus and rash abnormal hepatic enzyme and serum creatinine levels have also been reported.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk

balance of the medicinal product. 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

Symptoms of aceclofenac overdose include: headache, nausea, vomiting, epigastric pain, GI irritation, GI bleeding. Rarely diarrhoea, disorientation, excitation, coma, drowsiness, dizziness, tinnitus, hypotension, respiratory depression, fainting, and occasionally convulsions may occur. In cases of significant poisoning acute renal failure and liver damage are possible.
Treatment: If overdose with aceclofenac occurs, absorption should be prevented as soon as possible by means of gastric lavage and treatment with activated charcoal. Supportive and symptomatic treatment should be given for complications such as hypotension, renal failure, convulsions, GI irritation, and respiratory depression. Specific therapies such as forced diuresis, dialysis or haemoperfusion are probably of no help in eliminating NSAIDs due to their high rate of protein binding and extensive metabolism. Renal and liver function should be closely monitored.

Paracetamol Symptoms: Ingestion of 5 gram or more of paracetamol may lead to liver damage. Symptoms of paracetamol overdose in the first 24 hours are pallor, nausea, vomiting, anorexia and abdominal pain. Liver damage may become apparent 12 to 48 hours after ingestion. Abnormalities of glucose metabolism and metabolic acidosis may occur. In severe poisoning, hepatic failure may progress to encephalopathy, hemorrhage, hypoglycaemia, cerebral edema, and death. Acute renal failure with acute tubular necrosis, strongly suggested by loin pain, hematuria and proteinuria, may develop even in the absence of severe liver damage. Cardiac arrhythmias and pancreatitis have been reported.
Treatment: Immediate treatment is essential in the management of paracetamol overdose. Treatment with activated charcoal should be considered if the overdose has been taken within 1 hour. Plasma paracetamol concentration should be measured at 4 hours or later after ingestion (earlier concentrations are unreliable). Treatment with N-acetylcysteine (approved antidote) may be used up to 24 hours after ingestion of paracetamol. However, the maximum protective effect is obtained up to 8 hours post ingestion.

Chlorzoxazone Symptoms: Initial symptoms following chlorzoxazone overdose include gastrointestinal disturbances such as nausea, vomiting, or diarrhea together with drowsiness, dizziness, lightheadedness or headache may occur. Early in the course there may be malaise or sluggishness followed by marked loss of muscle tone, making voluntary movement impossible. The deep tendon reflexes may be decreased or absent. The sensorium remains intact, and there is no peripheral loss of sensation. Respiratory depression may occur with rapid, irregular respiration and intercostal and substernal retraction. There may be a decrease in blood pressure as well.
Treatment: Gastric lavage or induction of emesis should be carried out, followed by administration of activated charcoal. Thereafter, treatment is

entirely supportive. If respirations are depressed, oxygen and artificial respiration should be employed and a patent airway assured by use of an oropharyngeal airway or endotracheal tube. Hypotension may be counteracted by use of, plasma, concentrated albumin or a vasopressor agent such as norepinephrine.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Aceclofenac

ATC code: M01A B16,

Pharmacotherapeutic Group: Anti-inflammatory and anti-rheumatic preparations

Mechanism of action

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.

Paracetamol

ATC code: N02 BE01

Pharmacotherapeutic Group: General analgesics and antipyretics

Mechanism of action

In therapeutic doses paracetamol has antipyretic and mild analgesic action comparable to those of aspirin. It has no other important pharmacological effects and does not adversely affect platelet function and haemostasis.

Chlorzoxazone

ATC code: M03BB03

Pharmacotherapeutic Group: Centrally acting muscle relaxants

Mechanism of action

Chlorzoxazone is a centrally acting agent for painful musculoskeletal conditions. It acts primarily at the level of spinal cord and sub cortical areas of the brain where it inhibits multi synaptic reflex arcs involved in producing and maintaining skeletal muscle spasm of varied aetiology. The clinical result is reduction of the skeletal muscle spasm with relief of pain and increased mobility of the involved muscles. Blood level of chlorzoxazone can be detected in people during the first 30 minutes and peak level may be reached, in about 1 to 2 hour after oral administration.

5.2 Pharmacokinetic properties

Absorption

Aceclofenac: 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.

Paracetamol: Paracetamol is readily absorbed from the GI tract with peak plasma concentrations occurring about 30 minutes to 2 hours after ingestion.

Chlorzoxazone: Absorption of chlorzoxazone from the gastrointestinal tract is rapid and complete. Blood levels of chlorzoxazone can be detected in

humans during the first 30 minutes and peak levels occur approximately 1 to 2 hours after oral administration.

Distribution

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

Paracetamol: The elimination half-life varies from about 1 to 4 hours. Plasma protein binding is negligible at usual therapeutic concentrations but increases with increasing concentrations.

Chlorzoxazone: Chlorzoxazone is well distributed, with the highest concentrations found in plasma and fat, and lower concentrations found in the liver, muscle, brain and kidneys. The volume of distribution is roughly 14 L.

Metabolism

Aceclofenac: The main metabolite detected in plasma is 4'- hydroxy aceclofenac.

Paracetamol: Paracetamol is metabolized in the liver and excreted in the urine mainly as the glucuronide and sulphate conjugates. Less than 5% is excreted as unchanged paracetamol.

Chlorzoxazone: It is rapidly metabolised in the liver via the cytochrome P450 isoenzyme CYP2E1, mainly to 6- hydroxy chlorzoxazone.

Elimination

Aceclofenac: Approximately two- thirds of the administered dose is excreted via the urine, mainly as hydroxy metabolites. No changes in the pharmacokinetics of aceclofenac have been detected in the elderly.

Paracetamol: Paracetamol is metabolized in the liver and excreted in the urine mainly as the glucuronide and sulphate conjugates. Less than 5% is excreted as unchanged paracetamol.

Chlorzoxazone: 6- hydroxy chlorzoxazone is excreted in the urine primarily as the glucuronide metabolite. Less than 1% of a dose of chlorzoxazone is excreted unchanged in the urine in 24 hours; 74% of the metabolite is excreted within 10 hours. The elimination half-life of chlorzoxazone is about 1 hour.

5.3 Preclinical safety data

No data available.

6. Pharmaceutical particulars
6.1 List of Excipients:
ACLOSARA® MR

- Starch
- Micro Crystalline Cellulose
- Sodium Starch Glycolate
- PVPK-30
- Methyl Paraben Sodium
- Propyl Paraben Sodium
- Aerosil
- Purified Talc
- Magnesium Stearate
- Film Coat Material
- Methylene Dichloride
- PEG 6000
- Sunset Yellow Lake

6.2 Incompatibilities
Not Applicable

6.3 Shelf life
36 months.

6.4 Special precautions for storage
Store below 30°C. Protect from direct sunlight, heat & moisture.

6.5 Nature and contents of container
Aclosara® MR is available as 1 x 10 tablets in Alu-Alu blister pack.

6.6 Special precautions for disposal and other handling
Any unused medicine product or waste material should be disposed of in accordance with the local requirements.

7. Marketing authorization holder and manufacturing site addresses

Manufactured in India by:
Magbro Healthcare Pvt. Ltd
Located at village Mehsa Tibba,
P.O. Manjholi, The Nalagarh, Dist. Solan- 174101,
Himachal Pradesh, India.

Manufactured For & Marketed by:
KRISHNA CHEMISTS LTD.
P.O. BOX 3328-00506
NAIROBI, KENYA.

8. Marketing Authorization Number
CTD4409

9. Date of first authorization/renewal of the authorization
10. Date of revision of the text
11/02/2025