SUMMARY OF PRODUCT CHARACTERISTICS

1. Name of the medicinal product:

Diclosara® MR

Paracetamol, Chlorzoxazone & Diclofenac Sodium Tablets.

2. Qualitative and quantitative composition

Each uncoated tablet contains:

Paracetamol BP 325 mg

Chlorzoxazone USP 250 mg

Diclofenac Sodium BP 50 mg

Excipients q.s.

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

3. Pharmaceutical form:

Uncoated tablet

Yellow coloured, elongated shaped, biconvex uncoated tablets, one side break line and other side plain.

4. Clinical particulars

4.1. Therapeutic indications

Diclosara® MR tablet is indicated in soft tissue injuries with spasm and inflammation, neck/ shoulder/ back pain, tendonitis/tenosynovitis/bursitis Musculoskeletal disorders.

4.2. Posology and method of administration

Adults: One tablet to be taken 2 to 3 times daily or as directed by the physician.

Method of administration

For Oral use.

4.3. Contraindications

• Hypersensitivity to the active substance or any of the excipients.

• 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, angioedema, 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

The concomitant use with systemic NSAIDs including cyclooxygenase-2 selective inhibitors should be avoided due to the absence of any evidence demonstrating synergistic benefits and the potential for additive undesirable effects.

Gastrointestinal effects:

Gastrointestinal bleeding (haematemesis, melaena) ulceration or perforation which can be fatal has been reported with all NSAIDs including diclofenac and may occur at any time during treatment, with or without warning symptoms or a previous history of serious GI events. They generally have more serious consequences in the elderly. If gastrointestinal bleeding or ulceration occurs in patients receiving diclofenac, the drug should be withdrawn.

Close medical surveillance and caution should be exercised in patients with ulcerative colitis, or with Crohn's disease as these conditions may be exacerbated.

NSAIDs, including diclofenac, may be associated with increased risk of gastrointestinal anastomotic leak. Close medical surveillance and caution are recommended when using diclofenac after gastro-intestinal surgery.

Hepatic effects:

Close medical surveillance is required when prescribing to patients with impairment of hepatic function as their condition may be exacerbated.

As with other NSAIDs, including diclofenac, values of one or more liver enzymes may increase. During prolonged treatment with Diclofenac, regular monitoring of hepatic function is indicated as a precautionary measure.

Caution is called for when using diclofenac in patients with hepatic porphyria, since it may trigger an attack.

Renal effects:

As fluid retention and oedema have been reported in association with NSAIDs therapy, including diclofenac, particular caution is called for in patients with impaired cardiac or renal function, history of hypertension, the elderly, patients receiving concomitant treatment with diuretics or medicinal products that can significantly impact renal function, and those patients with substantial extracellular volume depletion from any cause, e.g. before or after major surgery. Monitoring of renal function is recommended as a precautionary measure when using diclofenac in such cases. Discontinuation therapy is usually followed by recovery to the pre-treatment state.

Skin effects:

Serious skin reactions, some of them fatal, including exfoliative dermatitis, Stevens-Johnson syndrome, toxic epidermal necrolysis and generalised bullous fixed drug eruption have been reported very rarely in association with the use of NSAIDs. Patients appear to be at the 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. Discontinuation of the therapy at the first appearance of skin rash, mucosal lesions or any other signs of hypersensitivity is recommended.

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.

Cardiovascular and cerebrovascular effects:

Patients with congestive heart failure (NYHA-I) or patients with significant risk factors for cardiovascular events (e.g. hypertension, hyperlipidaemia, diabetes mellitus, smoking) should only be treated with diclofenac after careful consideration.

As the cardiovascular risks of diclofenac 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.

Appropriate monitoring and advice are required for patients with a history of hypertension and congestive heart failure (NYHA-I) as fluid retention and oedema have been reported in association with NSAID therapy, including diclofenac.

Patients should remain alert for the signs and symptoms of serious arteriothrombotic events (e.g. chest pain, shortness of breath, weakness, slurring of speech), which can occur without warnings. Patients should be instructed to see a physician immediately in case of such an event.

Haematological effects:

During prolonged treatment with diclofenac, as with other NSAIDs, monitoring of the blood count is recommended.

Reversible inhibition of platelet aggregation has been noted. Patients with defects of haemostasis, bleeding diathesis or haematological abnormalities should be carefully monitored.

Pre-existing asthma:

In patients with asthma, seasonal allergic rhinitis, swelling of the nasal mucosa (i.e. nasal polyps), chronic obstructive pulmonary diseases or chronic infections of the respiratory tract (especially if linked to allergic rhinitis-like symptoms), reactions on NSAIDs like asthma exacerbations (so called intolerance to

analgesics / analgesics asthma), Quincke's oedema or urticaria are more frequent than in other patients. Therefore, special precaution is recommended in such patients (readiness for emergency). This is applicable as well for patients who are allergic to other substances, e.g. with skin reactions, pruritus or urticaria.

Like other drugs that inhibit prostaglandin synthetase activity, diclofenac sodium and other NSAIDs can precipitate bronchospasm if administered to patients suffering from, or with a previous history of bronchial asthma.

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

Diclofenac

Lithium: If used concomitantly, diclofenac may increase plasma concentrations of lithium. Monitoring of the serum lithium level is recommended.

Digoxin: If used concomitantly, diclofenac may raise plasma concentrations of digoxin. Monitoring of the serum digoxin level is recommended.

Diuretics and antihypertensive agents: Like other NSAIDs, concomitant use of diclofenac with diuretics and antihypertensive agents (e.g. betablockers, angiotensin converting enzyme (ACE) inhibitors may cause a decrease in their antihypertensive effect via inhibition of vasodilatory prostaglandin synthesis.

Drugs known to cause hyperkalemia: Concomitant treatment with potassium-sparing diuretics, ciclosporin, tacrolimus or trimethoprim may be associated with increased serum potassium levels, which should therefore be monitored frequently.

Anticoagulants and anti-platelet agents: Caution is recommended since concomitant administration could increase the risk of bleeding.

Other NSAIDs including cyclooxygenase-2 selective inhibitors and corticosteroids: Co-administration of diclofenac with other systemic NSAIDs or corticosteroids may increase the risk of gastrointestinal bleeding or ulceration. Avoid concomitant use of two or more NSAIDs.

Selective serotonin reuptake inhibitors (SSRIs): Concomitant administration of SSRI's may increase the risk of gastrointestinal bleeding.

Methotrexate: Diclofenac can inhibit the tubular renal clearance of methotrexate hereby increasing methotrexate levels. Caution is recommended when NSAIDs, including diclofenac, are administered less than 24 hours before treatment with methotrexate, since blood concentrations of methotrexate may rise and the toxicity of this substance be increase. Cases of serious toxicity have been reported when methotrexate and NSAIDs, including diclofenac are given within 24 hours of each other. This interaction is mediated through

accumulation of methotrexate resulting from impairment of renal excretion in the presence of the NSAID.

Ciclosporin: Diclofenac, like other NSAIDs, may increase the nephrotoxicity of ciclosporin due to the effect on renal prostaglandins. Therefore, it should be given at doses lower than those that would be used in patients not receiving ciclosporin.

Tacrolimus: Possible increased risk of nephrotoxicity when NSAIDs are given with tacrolimus. This might be mediated through renal anti-prostaglandin effects of both NSAID and calcineurin inhibitor.

Quinolone antibacterials: 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 an NSAID.

Phenytoin: When using phenytoin concomitantly with diclofenac, monitoring of phenytoin plasma concentrations is recommended due to an expected increase in exposure to phenytoin.

Colestipol and cholestyramine: These agents can induce a delay or decrease in absorption of diclofenac. Therefore, it is recommended to administer diclofenac at least one hour before or 4 to 6 hours after administration of colestipol/ cholestyramine.

Cardiac glycosides: Concomitant use of cardiac glycosides and NSAIDs in patients may exacerbate cardiac failure, reduce GFR and increase plasma glycoside levels.

Potent CYP2C9 inhibitors: Caution is recommended when co-prescribing diclofenac with potent CYP2C9 inhibitors (such as voriconazole), which could result in a significant increase in peak plasma concentrations and exposure to diclofenac due to inhibition of diclofenac metabolism.

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

Inhibition of prostaglandin synthesis may adversely affect the pregnancy and/or the embryo/foetal development. Data from epidemiological studies suggest an increased risk of miscarriage and or cardiac malformation and gastroschisis after use of a prostaglandin synthesis inhibitor in early pregnancy. The absolute risk for cardiovascular malformation was increased from less than 1% up to approximately 1.5%.

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

- cardiopulmonary toxicity (premature constriction/closure of the ductus arteriosus and pulmonary hypertension);

- renal dysfunction;

the mother and the neonate, at the end of the pregnancy, to:

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

- inhibition of uterine contractions resulting in delayed or prolonged labour. Consequently, Diclosara® MR is contraindicated during the third trimester of pregnancy.

Lactation

Like other NSAIDs, diclofenac passes into breast milk in small amounts. Therefore, diclofenac should not be administered during breast feeding in order to avoid undesirable effects in the infant.

4.7. Effects on ability to drive and use machines

Patients who experience visual disturbances, dizziness, vertigo, somnolence, central nervous system disturbances, drowsiness, or fatigue while taking NSAIDs should refrain from driving or operating machinery.

4.8. Undesirable effects

Diclosara® MR is well tolerated.

Diclofenac: Headache, dizziness. nausea, vomiting, diarrhoea. dyspepsia, abdominal pain, flatulence, anorexia are some common adverse events reported with diclofenac.

Paracetamol: Adverse effects of paracetamol are rare. Very rare cases of serious skin reactions have been reported.

Chlorzoxazone: Occasional patients may develop gastrointestinal disturbances.

Drowsiness, dizziness, light-headedness, malaise, or overstimulation may be noted by an occasional patient. Rarely, allergic-type skin rashes, petechiae, or ecchymoses may develop during treatment. Rarely, a patient may note discoloration of the urine resulting from phenol metabolites of chlorzoxazone.

Special population:

Elderly: The elderly are at increased risk of the serious consequences of adverse reactions. If a Diclosara® MR is considered necessary, the lowest effective dose should be used and for the short duration. The patient should be monitored for GI bleeding during NSAID therapy.

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 diclofenac overdose

There is no typical clinical picture resulting from diclofenac over dosage. Over dosage can cause symptoms such as headache, nausea, vomiting, epigastric pain, gastrointestinal bleeding, diarrhoea, dizziness, disorientation, excitation, coma, drowsiness, tinnitus, fainting or convulsions. In the case of significant poisoning acute renal failure and liver damage are possible.

Therapeutic measures

Management of acute poisoning with NSAIDs, including diclofenac, essentially consists of supportive measures and symptomatic treatment.

Supportive measures and symptomatic treatment should be given for complications such as hypotension, renal failure, convulsions, gastrointestinal disorder, and respiratory depression.

Special measures such as forced diuresis, dialysis or haemo-perfusion are probably of no help in eliminating NSAIDs, including diclofenac, due to high protein binding and extensive metabolism.

Activated charcoal may be considered after ingestion of a potentially toxic overdose, and gastric decontamination (e.g. vomiting, gastric lavage) after ingestion of a potentially life-threatening overdose

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

Diclofenac

ATC code: M01AB05,

Pharmacotherapeutic Group: Anti-inflammatory and anti-rheumatic, nonsteroids, Acetic acid derivatives and related substances.

Mechanism of action

Diclofenac is a non-steroidal agent with marked anti-inflammatory, antipyretic properties and analgesic properties. The mode of action of diclofenac is largely based on the inhibition to prostaglandin synthesis. Diclofenac is a potent inhibitor of the enzyme cyclo-oxygenase, which is involved in the production of prostaglandins, the mediators of inflammation. It also inhibits lipoxygenase thus preventing the synthesis of leukotrienes.

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.

Paracetamol reduces fever by a direct action on the heat regulating centres to increase the dissipation of heat.

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

Diclofenac: It is rapidly and almost completely absorbed when administered as oral dose, food does not have a significant effect on the extent of oral absorption.

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

Diclofenac: At therapeutic concentrations it is more than 99% bound to plasma proteins. Diclofenac and/or its metabolites are rapidly and preferentially taken up and retained in inflamed tissues. It penetrates synovial fluid where concentrations may persist even when plasma concentrations fall. The fluid terminal half fife is about l to 2 hours.

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

Diclofenac: Diclofenac is almost entirely metabolised in the liver. The biotransformation of diclofenac involves partly glucuronidation of the intact molecule but mainly single and multiple hydroxylation followed by glucuronidation.

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

Diclofenac: Approximately 60% of the dose administered is excreted in the urine in the form of metabolites, and less than 1% as unchanged substance. The remainder of the dose is eliminated as metabolites through the bile in the faeces.

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:

Starch Methyl Paraben Sodium

Di-Calcium Phosphate Propyl Paraben Sodium

Sodium Starch Glycollate Aerosil

Colour Tartrazine Purified Talcum

PVPK30 Magnesium Stearate

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

Diclosara® 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 AUTHORISATION HOLDER

Krishna Chemists Ltd

3rd Floor Metrix Hardware, Lusaka Road, Industrial Area.

8. MARKETING AUTHORISATION NUMBER(S)

H2017/CTD4464

9. DATE OF FIRST AUTHORISATION / RENEWAL OF THE AUTHORISATION

Date of first authorisation: 19.01.2026

10. DATE OF REVISION OF THE TEXT

19.01.2026