SUMMARY OF PRODUCT CHARACTERISTICS

1. **NAME OF THE MEDICINAL PRODUCT**
   CLODOL – 100 MG TABLETS
2. **QUALITATIVE AND QUANTITATIVE COMPOSITION**

   Each Enteric coated tablet contains Diclofenac Sodium 100 mg.

   For the full list of excipients, see section 6.1.

3. **PHARMACEUTICAL FORM**
   Delayed release Tablet

4.1 Therapeutic indications

It is used to treat Rheumatoid arthritis; osteoarthritis; low back pain; acute musculo-skeletal disorders and trauma such as periarthritis (especially frozen shoulder), tendinitis, tenosynovitis, bursitis, sprains, strains and dislocations; relief of pain in fractures; ankylosing spondylitis; acute gout; control of pain and inflammation in orthopaedic, dental and other minor surgery.

4.2. Posology and method of administration

Posology

Adults: One 100mg Diclofenac sodium tablet. If necessary, the daily dosage can be increased to 150 mg by supplementation with the dosage form containing Diclofenac sodium 25 mg or 50 mg. The recommended maximum daily dose of Diclofenac sodium is 150 mg.

Elderly: Although the pharmacokinetics of Diclofenac sodium are not impaired to any clinically relevant extent in elderly patients, nonsteroidal anti-inflammatory drugs should be used with particular caution in such patients who generally are more prone to adverse reactions. If Diclofenac sodium is considered necessary the lowest effective dosage should be used in frail elderly patients or those with a low body weight for the shortest possible duration. The patient should be monitored regularly for GI bleeding during NSAID therapy.

Renal impairment: Diclofenac sodium is contraindicated in patients with severe renal impairment. No specific studies have been carried out in patients with renal impairment, therefore, no specific dose adjustment recommendations can be made. Caution is advised when administering diclofenac to patients with mild to moderate renal impairment.

Hepatic impairment: Diclofenac is contraindicated in patients with severe hepatic impairment. No specific studies have been carried out in patients with hepatic impairment; therefore, no specific dose adjustment recommendations can be made. Caution is advised when administering diclofenac sodium to patients with mild to moderate hepatic impairment.

Paediatric population: Diclofenac sodium is not recommended for use in children as dosage recommendations and indications for use in this group of patients have not been established.

Method of administration

CLODOL 100 mg Tablet is swallowed whole with ample fluids. Patients with sensitive stomachs are advised to take CLODOL 100 mg Tablet with meals.

4.3 Contraindications

Known hypersensitivity to diclofenac sodium or to any of the excipients.
• Active gastric or intestinal ulcer, bleeding or perforation.
• History of gastrointestinal (GI) bleeding or perforation, related to previous non-steroidal anti-inflammatory drug (NSAID) therapy.
• Active or history of recurrent peptic ulcer or haemorrhage (two or more distinct episodes of proven ulceration or bleeding).
• Patients who have previously shown hypersensitivity reactions (e.g. asthma, rhinitis, angioedema or urticaria) in response to ibuprofen, aspirin, or other NSAIDs.
• Acute porphyria.
• Severe hepatic, renal or cardiac failure.
• During the last trimester of pregnancy.
• Established congestive heart failure (NYHA II-IV), ischaemic heart disease, peripheral arterial disease and/or cerebrovascular disease.

4.4 Special warnings and precautions for use

General:
Undesirable effects may be minimized by using the lowest effective dose for the shortest duration necessary to control symptoms.
Caution is indicated in the elderly on basic medical grounds. As with all NSAIDs, Diclofenac sodium should only be given to the elderly after other forms of treatment have been carefully considered, as the elderly have an increased frequency of adverse reactions to NSAIDs especially GI bleeding and perforation which may be fatal. In particular, it is recommended that the lowest effective dose be used in frail elderly patients or those with a low body weight.
The use of Diclofenac sodium with concomitant 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.
As with other NSAIDs, allergic reactions, including anaphylactic/anaphylactoid reactions, can also occur in rare cases with diclofenac without earlier exposure to the drug.
Like other NSAIDs, diclofenac may mask the signs and symptoms of infection due to its pharmaco dynamic properties.

Gastrointestinal effects:
GI bleeding, ulceration or perforation, which can be fatal, has been reported with NSAID therapy, including diclofenac, and can 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 GI bleeding or ulceration occurs in patients receiving Diclofenac sodium, the treatment should be withdrawn.
As with all NSAIDs, including diclofenac sodium, close medical surveillance is imperative and particular caution should be exercised when prescribing diclofenac sodium in patients with symptoms indicative of GI disorders or with a history suggestive of gastric or intestinal ulceration, bleeding or perforation. 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.
To reduce the risk of GI toxicity in patients with a history of ulcer, particularly if complicated with haemorrhage or perforation, and in the elderly, the treatment should be initiated and maintained at the lowest effective dose.
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 GI risk.
Patients with a history of GI toxicity, particularly the elderly, should report any unusual abdominal symptoms (especially GI bleeding) particularly in the initial stages of treatment.
Caution is advised in patients receiving concomitant medications that could increase the risk of ulceration or bleeding, such as systemic corticosteroids, anticoagulants such as warfarin, anti-platelet agents such as aspirin or selective serotonin-reuptake inhibitors.
Close medical surveillance and caution should also be exercised in patients with ulcerative colitis or Crohn's disease, as their condition may be exacerbated.

Hepatic effects:

Close medical surveillance is required when prescribing Diclofenac sodium to patients with impaired hepatic function, as their condition may be exacerbated.
As with other NSAIDs, including diclofenac sodium, values of one or more liver enzymes may increase. During prolonged treatment with Diclofenac sodium, regular monitoring of hepatic function is indicated as a precautionary measure. If abnormal liver function tests persist or worsen, if clinical signs or symptoms consistent with liver disease develop, or if other manifestations occur (e.g. eosinophilia, rash), Diclofenac sodium should be discontinued. Hepatitis may occur with use of diclofenac sodium without prodromal symptoms.
Caution is called for when using Diclofenac sodium in patients with hepatic porphyria, since it may trigger an attack.

Renal effects:

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 and the elderly.
As fluid retention and oedema have been reported in association with NSAID therapy, including diclofenac sodium, 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 in 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 sodium in such cases. Discontinuation of therapy is usually followed by recovery to the pre-treatment state.

Cardiovascular and cerebrovascular effects:

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 sodium 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.
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.
Clinical trial and epidemiological data consistently point towards an increased risk of arterial thrombotic events (for example myocardial infarction or stroke) associated with the use of diclofenac sodium, particularly at high dose (150mg daily) and in long term treatment.

Respiratory disorders:
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. Caution is required if administered to patients suffering from, or with a previous history of, bronchial asthma, since NSAIDs have been reported to cause bronchospasm in such patients.
Haematological:
During prolonged treatment with diclofenac sodium, as with other NSAIDs, monitoring of the blood count is recommended.
Diclofenac sodium, in common with other NSAIDs, can reversibly inhibit platelet aggregation. Patients with defects of haemostasis should be carefully monitored.
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.
Dermatological:
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 for these reactions early in the course of therapy: the onset of reaction occurring in the majority of cases within the first month of treatment. Diclofenac sodium should be discontinued at the first appearance of skin rash, mucosal lesions or any other sign of hypersensitivity.
Impaired Female fertility:
The use of Diclofenac sodium may impair female fertility and is not recommended in women attempting to conceive. In women who have difficulties conceiving or who are undergoing investigation of infertility, withdrawal of Diclofenac sodium should be considered.
Interaction with other medicinal products and other forms of interaction
Lithium: Diclofenac sodium may increase plasma concentrations and decrease elimination of lithium. Monitoring of the serum lithium level is recommended.
Cardiac glycosides: NSAIDs may exacerbate cardiac failure and reduce GFR. If used concomitantly, diclofenac sodium may raise plasma concentrations of digoxin. Monitoring of the serum digoxin level is recommended.
Anticoagulants and anti-platelet agents: Caution is recommended since concomitant administration could increase the risk of bleeding Although clinical investigations do not appear to indicate that diclofenac sodium affects the action of anticoagulants, there are reports of an increased risk of haemorrhage in patients receiving diclofenac sodium and anticoagulants concomitantly. Close monitoring of such patients is therefore recommended.
Antidiabetic agents: Clinical studies have shown that Diclofenac sodium can be given together with oral hypoglycaemic agents without influencing their clinical effect. However, there have been isolated reports of hyperglycaemic and hypoglycaemic effects, which have required adjustments to the dosage of hypoglycaemic agents. For this reason, monitoring of the blood glucose level is recommended as a precautionary measure during concomitant therapy.

Ciclosporin: Ciclosporin nephrotoxicity may be increased by the effect of NSAIDs, including diclofenac sodium, on renal prostaglandins. Therefore, Diclofenac sodium should be given at doses lower than those that would be used in patients not receiving ciclosporin.
Mifepristone: NSAIDs should not be used for 8-12 days after mifepristone administration as NSAIDs can reduce the effect of mifepristone.
Methotrexate: Diclofenac sodium can inhibit the tubular renal clearance of methotrexate thereby increasing methotrexate levels. Caution should be exercised if NSAIDs, including diclofenac,and methotrexate are administered within 24 hours of each other, since NSAIDs may increase methotrexate plasma levels with decreased elimination, resulting in increased toxicity.
Quinolone antibiotics: Animal data indicate that NSAIDs can increase the risk of convulsions associated with quinolone antibiotics. Patients taking NSAIDs and quinolones may have an increased risk of developing convulsions. There have been isolated reports of convulsions which may have been due to concomitant use of quinolones and NSAIDs.
Selective serotonin reuptake inhibitors (SSRIs): Increased risk of GI bleeding.
Other analgesics including cyclooxygenase-2 selective inhibitors: Avoid concomitant use of two or more systemic NSAIDs (including aspirin) as this may increase the risk of adverse events.
Corticosteroids: Systemic corticosteroids can increase the risk of GI ulceration or bleeding.
Diuretics and antihypertensive agents: Like other NSAIDs, concomitant use of diclofenac sodium with diuretics or antihypertensive agents (e.g. beta-blockers, angiotensin converting enzyme (ACE) inhibitors) may cause a decrease in their antihypertensive effect. Therefore, the combination should be administered with caution and patients, especially the elderly, should have their blood pressure periodically monitored. Patients should be adequately hydrated and consideration should be given to monitoring of renal function after initiation of concomitant therapy and periodically thereafter, particularly for diuretics and ACE inhibitors due to the increased risk of nephrotoxicity. Concomitant treatment with potassium-sparing drugs may be associated with increased serum potassium levels, which should therefore be monitored frequently.
Tacrolimus: Possible increased risk of nephrotoxicity when NSAIDs are given with tacrolimus.
Zidovudine: Increased risk of haematological toxicity when NSAIDs are given with zidovudine. There is evidence of an increased risk of haemarthroses and haematoma in HIV (+) haemophiliacs receiving concurrent treatment with zidovudine and ibuprofen.
Phenytoin: When using phenytoin concomitantly with diclofenac sodium, monitoring of phenytoin plasma concentrations is recommended due to an expected increase in exposure to phenytoin.
Colestipol and colestyramine: 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 or colestyramine.
Potent CYP2C9 inhibitors: Caution is recommended when co-prescribing diclofenac sodium with potent CYP2C9 inhibitors (such as voriconazole), which could result in a significant increase in peak plasma concentration and exposure to diclofenac sodium due to inhibition of diclofenac metabolism.
Pregnancy:
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 of 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%.
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 pre- and post implantation 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, diclofenac sodium should not be given unless clearly necessary. If diclofenac sodium 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 oftreatment as short as possible.
During the third trimester of pregnancy, all prostaglandin synthesis inhibitors may expose the foetus to:
- cardiopulmonary toxicity (with premature closure of the ductus arteriosus and pulmonary hypertension);
- renal dysfunction, which may progress to renal failure with oligohydramnios; the mother and the neonate, at the end of 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, diclofenac sodium is contraindicated during the third trimester of pregnancy.
Lactation:
In limited studies so far available, diclofenac can appear in breast milk in very low concentrations with traces of diclofenac sodium found in breast milk following oral doses of 50mg every eight hours. Therefore, diclofenac sodium should not be administered during breastfeeding in order to avoid undesirable effects in the infant.
Fertility:
The use of diclofenac may impair female fertility and is not recommended in women attempting to conceive. In women who have difficulties conceiving or who are undergoing investigation of infertility, withdrawal of diclofenac should be considered.

4.5 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.
Undesirable effects
Adverse reactions are ranked under the heading of frequency, the most frequent first, using the following convention: very common: (>1/10); common (≥ 1/100, <1/10); uncommon (≥ 1/1,000, <1/100); rare (≥1/10,000, <1/1000); very rare (<1/10,000); not known: cannot be estimated from the available data.
The following undesirable effects include those reported with either short-term or long-term use.

Blood and lymphatic system disorders	
Very rare	Thrombocytopenia, leucopoenia, anaemia (including haemolytic and aplastic anaemia), agranulocytosis
Immune system disorders	
Rare	Hypersensitivity, anaphylactic and anaphylactoid reactions (including hypotension and shock).
Very rare	Angioneurotic oedema (including face oedema).
Psychiatric disorders	
Very rare	Disorientation, depression, insomnia, nightmare, irritability, psychotic disorder.
Nervous system disorders	
Common	Headache, dizziness.
Rare	Somnolence, tiredness.
Very rare	Paraesthesia, memory impairment, convulsion, anxiety, tremor, aseptic meningitis, taste disturbances, cerebrovascular accident.
Unknown	Confusion, hallucinations, disturbances of sensation, malaise.
Eye disorders	
Very rare	Visual disturbance, vision blurred, diplopia.
Unknown	Optic neuritis.
Ear and labyrinth disorders	
Common	Vertigo.
Very rare	Tinnitus, hearing impaired
Cardiac disorders	
Uncommon*	Palpitations, chest pain, cardiac failure, myocardial infarction.
Vascular disorders	
Very rare	Hypertension, hypotension, vasculitis.
Respiratory, thoracic and mediastinal disorders	
Rare	Asthma (including dyspnoea).
Very rare	Pneumonitis.
Gastrointestinal disorders	
Common	Nausea, vomiting, diarrhoea, dyspepsia, abdominal pain, flatulence, anorexia.
Rare	Gastritis, gastrointestinal haemorrhage, haematemesis, diarrhoea haemorrhagic, melaena gastrointestinal ulcer with or without bleeding or perforation (sometimes fatal particularlyin the elderly).
Very rare	Colitis (including haemorrhagic colitis and exacerbation of ulcerative colitis or Crohn's disease), constipation, stomatitis (including ulcerative stomatitis), glossitis, oesophageal disorder, diaphragm-like intestinal strictures, pancreatitis.
Unknown	Ischaemic colitis
Hepatobiliary disorders	
Common	Transaminases increased.
Rare	Hepatitis, jaundice, liver disorder.
Very rare	Fulminant hepatitis, hepatic necrosis, hepatic failure.

Skin and subcutaneous tissue disorders	
Common	Rash.
Rare	Urticaria.
Very rare	Bullous eruptions, eczema, erythema, erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis (Lyell's syndrome), dermatitis exfoliative, loss of hair, photosensitivity reaction, purpura, allergic purpura, pruritus.
Renal and urinary disorders	
Very rare	Acute renal failure, haematuria, proteinuria, nephrotic syndrome, interstitial nephritis, repapillary necrosis.
General disorders and administration site conditions	
Rare	Oedema
Reproductive system and breast disorders	
Very rare	Impotence.

*The frequency reflects data from long-term treatment with a high dose (150 mg/day).

Clinical trial and epidemiological data consistently point towards an increased risk of arterial thrombotic events (for example myocardial infarction or stroke) associated with the use of diclofenac sodium, particularly at high dose (150mg daily) and in long term treatment.

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 by emailing on FDA site, fda@fdaghana.gov.gh

4.6 Overdose

A) Symptoms

There is no typical clinical picture resulting from diclofenac sodium over dosage. Symptoms include headache, nausea, vomiting, epigastric pain, gastrointestinal bleeding, rarely diarrhoea, disorientation, excitation, coma, drowsiness, dizziness, tinnitus, fainting and occasionally convulsions. In cases of significant poisoning acute renal failure and liver damage are possible.

B) Therapeutic measures

Management of acute poisoning with NSAIDs, including diclofenac sodium, 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 sodium, due to high protein binding and extensive metabolism.

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

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.

Frequent or prolonged convulsions should be treated with intravenous diazepam.

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

5.1. Pharmacodynamic properties

Pharmacotherapeutic group: Acetic acid derivatives and related substances, ATC code: M01AB05.
Mechanism of action
Diclofenac sodium is a non-steroidal agent with marked analgesic/anti-inflammatory properties. It is an inhibitor of prostaglandin synthetase, (cyclo-oxygenase).
Diclofenac sodium in vitro does not suppress proteoglycan biosynthesis in cartilage at concentrations equivalent to the concentrations reached in human beings.

PHARMACOKINETICS PROPERTIES

Diclofenac sodium is slowly but fully absorbed from enteric coated tablets. It is subject to first pass metabolism so that about 50% of the drug reaches the systemic circulation in the unchanged form. The terminal plasma half life is about 1 to 2 hours. Diclofenac is metabolized to 4'-hydroxydiclofenac, 5-hydroxydiclofenac, 3'-hydroxydiclofenac, 4.,5-dihydroxydiclofenac. It is then excreted in the form of glucuronide and sulfate conjugate, mainly in the urine (about 65%) but also in the bile (about 35%).

Overdose
(a) Symptoms
There is no typical clinical picture resulting from diclofenac sodium over dosage. Symptoms can include headache, nausea, vomiting, epigastric pain, GI bleeding, diarrhoea, disorientation, excitation, coma, drowsiness, dizziness, tinnitus, fainting, or convulsions. In cases of significant poisoning, acute renal failure and liver damage are possible.
(b) 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, GI disorder, and respiratory depression.
Special measures such as forced diuresis, dialysis or haemo-perfusion are probably of no help in eliminating NSAIDs, including diclofenac sodium, due to the 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.
Renal and liver function should be closely monitored.
Patients should be observed for at least four hours after ingestion of potentially toxic amounts.
Frequent or prolonged convulsions should be treated with intravenous diazepam.
Other measures may be indicated by the patient's clinical condition.

6.1 List of excipients

Maize starch, Lactose, Talcum, Magnesium stearate, Cellulose acetate phthalate, Sunset yellow colour. Methyl Paraben, Propyl paraben, microcrystalline cellulose, Sodium starch glycollate.

6.2 Incompatibilities

Not applicable

6.3 Shelf life

2 years

6.4. Special precautions for storage

Do not store above 30°C

6.5 Nature and contents of container

Aluminium foil/PVC blister strips: Pack sizes 10 Tablets

Blister strips consisting of 0.02 mm thick aluminium foil with a form packing bottom strip of 0.25mm clear PVC.

Pack sizes: 10 Tablets

Inner box of 1x10 tablets

Outer box of 1x10x10 tablets.

6.6. Special precautions for disposal

No special requirements

7. MARKETING AUTHORISATION HOLDER

ESKAY THERAPEUTICS LTD

P.O.BOX 431

DARKUMAN

8.MARKETING AUTHORISATION NUMBER(S)

FDA/SD.093-9122.

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

JULY 1 .2024.

10. DATE OF REVISION OF THE TEXT

Jun- 2019

11. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.