SUMMARY PRODUCT CHARACTERISTICS

1. Name of the medicinal product

GOMBEFENAC (DICLOFENAC POTASSIUM TABLETS 50 MG)

2. Qualitative and quantitative composition

Each Film coated tablet contains:

Diclofenac Potassium BP…..50 mg

Excipients……..q.s

Colour: Brilliant blue, Tartrazine, Indigo Carmine

3. Pharmaceutical form

Solid oral dosage form

4. Clinical particulars

4.1 Therapeutic indications

Relief of all grades of pain and inflammation in a wide range of conditions, including: arthritic conditions: rheumatoid arthritis, osteoarthritis, ankylosing spondylitis, acute gout, acute muscular-skeletal disorders such as per arthritis (for example frozen shoulder), tendinitis, tenosynovitis, bursitis, other painful conditions resulting from trauma, including fracture, low back pain, sprains, strains, dislocations, orthopedic, dental and other minor surgery.

Children:

Diclofenac Potassium Tablets 50 mg are not suitable for children.

4.2 Posology and method of administration

Adult men (aged 18 to 64 years)

5 mg to 150 mg daily in two or three divided doses. The recommended maximum daily dose of Diclofenac Potassium Tablets 50 mg

Elderly (age 65 years and over)

Although the pharmacokinetics of Diclofenac Potassium are not impaired to any clinically relevant extent in elderly patients, no steroidal anti-inflammatory drugs should be used with particular caution in such patients who generally are more prone to adverse reactions. In

particular it is recommended that the lowest effective dosage be used in frail elderly patients or those with a low body weight (see also precautions) and the patient should be monitored for GI bleeding during NSAID therapy over.

Cardiovascular and significant cardiovascular risk factors

Diclofenac is contraindicated in patients with established congestive heart failure (NYHA II-IV), ischemic heart disease, peripheral arterial disease and/or cerebrovascular disease.

Paediatric population

Diclofenac Potassium Tablets 50 mg are not suitable for children.

Patients with 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

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients Active, gastric or intestinal ulcer, bleeding or perforation. History of gastrointestinal bleeding or perforation, relating to previous NSAIDs therapy. Active or history of recurrent peptic ulcer/hemorrhage (two or more distinct episodes of proven ulceration or bleeding. Last trimester of pregnancy Hepatic failure, renal failure.

4.4 Special warnings and precautions for use

Warnings and precautions:

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

Other forms of sexual dysfunction: Lactose This medicine contains lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

Sodium : This medicine contains less than 1 m mol sodium (23 mg) per tablet, that is to say essentially 'sodium-free'. Suicide/suicidal thoughts:

Gastrointestinal effects: Gastrointestinal bleeding (haematemesis, melaena), ulceration or perforation, which can be fatal has been reported with all NSAIDs including Diclofenac Potassium and may occur at any time during treatment, with or without warning symptoms or a

previous history of serious gastrointestinal (GI) events. They generally have more serious consequences in the elderly. If gastrointestinal bleeding or ulceration occurs in patients receiving Diclofenac, the medicinal product should be withdrawn.

Renal impairment: As fluid retention and edema have been reported in association with NSAID 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 in those patients with substantial extracellular volume depletion from any cause, e.g. before or after major surgery

Skin effects: 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, including Diclofenac Sodium and Paracetamol

Hematological effects: During prolonged treatment with Diclofenac, as with other NSAIDs, monitoring of the blood count is recommended.

Pre-existing asthma: Like other drugs that inhibit prostaglandin synthesize activity, Diclofenac Potassium and other NSAIDs can precipitate bronchospasm if administered to patients suffering from, or with a previous history of bronchial asthma.

Female fertility: The use of Diclofenac may impair female fertility and is not recommended in women attempting to conceive. In women who may have difficulties conceiving or who are undergoing investigation of infertility, withdrawal of Diclofenac should be considered.

4.5 Interaction with other medicinal products and other forms of interaction

Pharmacodynamic interactions:-

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

Dioxin: If used concomitantly, Diclofenac may raise plasma concentrations of dioxin. Monitoring of the serum dioxin level is recommended. Diuretics and Anti-hypertensive agents: Like other SAIDs, concomitant use of Diclofenac with diuretics or antihypertensive agents (e.g. beta- blockers, angiotensin converting enzyme (ACE) inhibitors) may cause a decrease in their antihypertensive effect via inhibition of vasodilator prostaglandin synthesis. 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.

Drugs known to cause hypokalemia: 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 Although clinical investigations do not appear to indicate that Diclofenac affects the action of anticoagulants, there are reports of an increased risk of hemorrhage in patients receiving Diclofenac and anticoagulants concomitantly Therefore, to be certain that no change in anticoagulant dosage is required, close monitoring of such patients is required. As with other no steroidal anti-inflammatory agents, Diclofenac in high dose can reversibly inhibit platelet aggregation

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

Ant diabetics: Clinical studies have shown that Diclofenac Potassium can be given together with oral ant diabetic agents without influencing their clinical effect. However, there have been isolated reports of hypoglycemic and hyperglycemic effects necessitating changes in the dosage of the ant diabetic agents during treatment with Diclofenac Sodium and Paracetamol. For this reason, monitoring of the blood glucose level is recommended as a precautionary measure during concomitant therapy.

4.6 Fertility, pregnancy and Breast feeding

Pregnancy:

Inhibition of prostaglandin synthesis may adversely affect the pregnancy and/or the embryo/fetal 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-fetal lethality.

Breast feeding:

Like other NSAIDs, Diclofenac Potassium passes into the breast milk in small amounts. Therefore, Diclofenac should not be administered during breast feeding in order to avoid undesirable effects in the infant. As with other NSAIDs, the use of Diclofenac Potassium 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

4.7 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 operate machinery.

4.8 Undesirable effects

Sudden and crushing chest pain (signs of myocardial infarction or heart attack) Breathlessness, difficulty breathing when lying down, swelling of the feet or legs (signs of heart failure) Sudden weakness or numbness in the face, arm or leg especially on one side of the body, sudden loss or disturbance of vision; sudden difficulty in speaking or ability to understand speech; sudden migraine-like headaches which happen for the first time, with or without disturbed vision. These symptoms can be an early sign of a stroke. Stomach pain, indigestion, heartburn, wind, nausea (feeling sick) or vomiting (being sick)Any sign of bleeding in the stomach or intestine, for example, when emptying your bowels, blood in vomit or black, tarry faeces Allergic reactions which can include skin rash, itching, bruising, painful red areas, peeling or blistering.

Common side effects (These may affect between 1 and 1 in 10 in every 100 patients):

Stomach pain, heartburn, nausea, vomiting, diarrhea, indigestion, wind, loss of appetite Headache, dizziness, vertigo, Skin rash or spots, Raised levels of liver enzymes in the blood

Uncommon side effects (These may affect between 1 and 10 in every 1000 patients):

Fast or irregular heart beat (palpitations), chest pain, heart disorders, including heart attack or breathlessness, difficulty breathing when lying down, or swelling of the feet or legs (signs of heart failure).

4.9 Overdose

There is no typical clinical picture resulting from Diclofenac Potassium over dosage. Over dosage can cause symptoms such as headache, nausea, vomiting, epigastria pain, gastrointestinal hemorrhage, diarrhea, 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 Potassium 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 dieresis, dialysis or haemoid-perfusion are probably of no help in eliminating NSAIDs, including Diclofenac Potassium 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

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Acetic acid derivatives and related substances,

ATC code: M01AB05

Mechanism of action: Diclofenac Potassium is a non-steroidal agent with marked analgesic/anti-inflammatory properties. It is an inhibitor of prostaglandin synthesizes, (cycloxygenase).Diclofenac Potassium in vitro does not suppress proteoglycan biosynthesis in cartilage at concentrations equivalent to the concentrations reached in human beings.

5.2 Pharmacokinetic properties

Absorption

Absorption is complete but onset is delayed until passage through the stomach, which may be affected by food which delays stomach emptying. The mean peak plasma Diclofenac concentration reached at about 2 hours (50mg dose produces 1511± 466 Mg/ml).

Distribution

The active substance is 99.7% protein bound; mainly to albumin (99.4%). Diclofenac Potassium enter the synovial fluid, where maximum concentrations are measured 2-4 hours after the peak

plasma values have been attained. The apparent half-life for elimination from the synovial fluid is 3-6 hours. Two hours after reaching the peak plasma values, concentrations of the active substance are already higher in the synovial fluid than they are in the plasma and remain higher for up to 12 hours.

Biotransformation

Biotransformation of Diclofenac Potassium takes place partly by glucuronidation of the intact molecule, but mainly by single and multiple hydroxylation and methoxylation, resulting in several phenol metabolites, most of which are converted to glucuronide conjugates. Two phenol metabolites are biologically active, but to a much lesser extent than Diclofenac.

Elimination

The total systemic clearance of Diclofenac Potassium in plasma is 263 ± 56 mL/min (mean value ± SD). The terminal half-life in plasma is 1-2 hours. Four of the metabolites, including the two active ones, also have short plasma half-lives of 1-3 hours. About 60% of the administered dose is excreted in the urine in the form of the glucuronide conjugate of the intact molecule and as metabolites, most of which are also converted to glucuronide conjugates. Less than 1% is excreted as unchanged substance. The rest of the dose is eliminated as metabolites through the bile in the faces.

5.3 Preclinical safety data

Not applicable

6. Pharmaceutical particulars

6.1 List of Excipients

Microcrystalline cellulose Maize starch Dibasic Calcium Phosphate Isopropyl Alcohol Povidone K-30 Magnesium stearate Purified Talc Colloidal anhydrous silica Croscarmellose sodium Colour Brilliant Blue Isopropyl Alcohol Methylene Chloride.

6.2 Incompatibilities

Not applicable

6.3 Shelf life: 3 YEAR

6.4 Special precautions for storage

Do not store above 25°C.

6.5 Nature and contents of container

Blister of 10 tablets packed in a monocarton, such 10 Monocarton are packed in a carton along with Pack insert.

6.6 Special precautions for disposal and other handling

Not applicable

7. Product of

KESAR PHARMA (P) LIMITED

Plot Survey No.50-P/2, Po Chhatral. Gandhinagar, INDIA

8. Marketing authorization holder

Berlin Pharma & Healthcare Ltd.
42, Comfort Oboh, Kiri-Kiri industrial Area. Apapa-Lagos, Nigeria.

9. Marketing authorization number(s)

NAFDAC REG. NO.: B4 - 7142

10. Date of first authorization/renewal of the authorization

Not Applicable

11. Date of revision of the text:

Not Applicable