1. Name of the medicinal product

Diclofenac Potassium And Paracetamol Tablets (Dicgem Tablets)

2. Qualitative and quantitative composition

Each Uncoated tablet contains:
Diclofenac Potassium BP……50 mg
Paracetamol BP……...500 mg
Excipients…….qs

3. Pharmaceutical form

Uncoated tablet
White colour oval shape biconvex one side embossed "DICGEM" and other side break line uncoated tablet.

4. Clinical particulars

4.1 Therapeutic indications

Adults and elderly

Relief of all grades of pain and inflammation in a wide range of conditions, including:

(i) arthritic conditions: rheumatoid arthritis, osteoarthritis, ankylosing spondylitis, acute gout,

(ii) acute musculo-skeletal disorders such as periarthritis (for example frozen shoulder), tendinitis, tenosynovitis, bursitis,

(iii) other painful conditions resulting from trauma, including fracture, low back pain, sprains, strains, dislocations, orthopaedic, dental and other minor surgery.

Children

Diclofenac Potassium And Paracetamol Tablets are not suitable for children.

4.2 Posology and method of administration

Posology

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

Adults: 75 mg to 150 mg daily in two or three divided doses.

The recommended maximum daily dose of diclofenac potassium is 150mg.

Special populations

Elderly:

Although the pharmacokinetics of diclofenac potassium 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. In particular it is recommended that the lowest effective dosage be used in frail elderly patients or those with a low body weight and the patient should be monitored for GI bleeding during NSAID therapy.

Cardiovascular and significant cardiovascular risk factors

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

Patients with congestive heart failure (NYHA-I) or significant risk factors for cardiovascular disease should be treated with diclofenac only after careful consideration. Since cardiovascular risks with diclofenac may increase with dose and duration of exposure, the lowest effective daily dose should be used and for the shortest duration possible

Renal impairment: Diclofenac potassium is contraindicated in patients with renal failure. 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.

Paediatric population:

Diclofenac potassium and paracetamol tablets are not suitable for children.

Method of administration

For oral administration.

To be taken whole with liquid, preferably with or after food.

4.3 Contraindications

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

• Active, or 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/haemorrhage (two or more distinct episodes of proven ulceration or bleeding).

• Last trimester of pregnancy

• Hepatic failure

• Renal failure

• Established congestive heart failure (NYHA-II-IV), ischemic heart disease, peripheral arterial disease and/or cerebrovascular disease.

• Like other non-steroidal anti-inflammatory drugs (NSAIDs), diclofenac is also contraindicated in patients in whom attacks of asthma, angiodema, urticaria or acute rhinitis are precipitated by ibuprofen, acetylsalicylic acid or other nonsteroidal anti-inflammatory drugs.

4.4 Special warnings and precautions for use

Diclofenac Potassium & Paracetamol Tablets should be taken with extreme caution to prevent some side effects and to maximize the benefits. The following points should be considered while taking the medication:

- Do not crush, chew, or break the tablet instead swallow this tablet as a whole.
- Take diclofenac potassium & paracetamol tablets with food.
- Avoid the consumption of any alcoholic beverage while taking the medicine.
- In the case of pregnancy, the medicine has more potential risks than benefits.
- The medication can affect the ability to drive so driving should be avoided.

Therefore, these are some considerable points about Diclofenac Potassium and Paracetamol Tablet. Further, the medication should be used as per the directions of the doctor, or physician for the best possible effects.

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

Drug-Drug Interaction: DICLOFENAC+PARACETAMOL is shown to interact with various drugs. Some of them include pain killers (naproxen, aspirin, ibuprofen, tramadol, hydrocodone, oxycodone), antibiotics (ciprofloxacin, levofloxacin, moxifloxacin, nalidixic acid, norfloxacin or ofloxacin), diuretics (furosemide and bumetanide), medicines for heart problems or medicines for high blood pressure (digoxin), medicines used to lower cholesterol (colestipol and cholestyramine), medicines to treat seizures (phenytoin), medicines that reduce the activity of your immune system (ciclosporin or tacrolimus), steroid medicines (hydrocortisone or prednisolone), blood thinner (warfarin), anti-depressant (duloxetine) and acidity lowering drugs (cimetidine). These drugs may affect the working of DICLOFENAC+PARACETAMOL and may alter its efficacy.

Drug-Food Interaction: Excessive intake of caffeine-containing food or drinks like coffee, tea, chocolate and some fizzy drinks should be avoided while taking DICLOFENAC+PARACETAMOL. Taking together may lead to drowsiness and dizziness and sleepiness.

Drug-Disease Interaction: DICLOFENAC+PARACETAMOL should not recommend for people with asthma, urticaria or acute rhinitis as the attacks precipitate with the use of NSAIDs.

4.6 Fertility, pregnancy and lactation
Pregnancy:

Dicgem Tablets should not be taken during pregnancy without doctor’s permission.

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. If diclofenac 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 of treatment 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 oligo-hydroamniosis;

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.

Breast-feeding:

Like other NSAIDs, diclofenac 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

Femaile Fertility

As with other NSAIDs, 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 (see also section 4.4 regarding female fertility).

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

Adverse reactions (Table 1) are ranked under 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, <1/1,000); very rare (<1/10,000); Not known: cannot be estimated from the available data.

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, particularly at high dose (150 mg daily) and in long term treatment (see sections 4.3 and 4.4).

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.

4.9 Overdose

Symptoms

There is no typical clinical picture resulting from diclofenac over dosage. Over dosage can cause symptoms such as headache, nausea, vomiting, epigastric pain, gastrointestinal haemorrhage, 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 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

Non-steroidal anti-inflammatory drugs (NSAlDs).

Mechanism of action:

Diclofenac potassium and paracetamol is a non-steroidal agent with marked analgesic/anti inflammatory properties. It is an inhibitor of prostaglandin synthetase, (cyclo-oxygenase).

Diclofenac potassium and paracetamol 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 potassium concentration reached at about 2 hours (50mg dose produces 1511± 466 ng/ml).

Bioavailability:

About half of the administered diclofenac is metabolised during its first passage through the liver ("first-pass" effect), the area under the concentrations curve (AUC) following oral administration is about half that following an equivalent parenteral dose.

Pharmacokinetic behaviour does not change on repeated administration. Accumulation does not occur, provided the recommended dosage intervals are observed.

Distribution

The active substance is 99.7% protein bound, mainly to albumin (99.4%).

Diclofenac potassium enters 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.Diclofenac potassium was detected in a low concentration (100 ng/mL) in breast milk in one nursing mother. The estimated amount ingested by an infant consuming breast milk is equivalent to a 0.03 mg/kg/day dose.

Metabolism

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

Elimination

The total systemic clearance of diclofenac 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 faeces.

5.3 Preclinical safety data
None stated.

6. Pharmaceutical particulars

6.1 List of excipients
Starch
PVPK-30
Methyl Paraben Sodium
Propyl Paraben Sodium
Talcum
Magnesium Stearate
Aerosil
Sodium starch glycolate

6.2 Incompatibilities
Not applicable.

6.3 Shelf life
4 years.

6.4 Special precautions for storage
Store in a cool, dry place. Protect from light. Keep all medicines out of reach of children.

6.5 Nature and contents of container
100x10x1x10 Tabs

6.6 Special precautions for disposal and other handling
No special requirements.