## 1.0 NAME OF THE MEDICINAL PRODUCT

EGMP Diclofenac Potassium 50 mg Caplets

## 2.0 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains:
Diclofenac Potassium 50mg
Excipient(s) with known effect:
For the full list of excipients, see section 6.1.

## 3.0 PHARMACEUTICAL FORM

Oral administration

## 4.0 CLINICAL PARTICULARS

### 4.1 Therapeutic indications

Rheumatoid arthritis
Osteoarthrosis
Low back pain
Migraine attacks
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
Pyrophosphate arthropathy and associated disorders

### 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 (see section 4.4 Special warnings and precautions for use).

**Adults**

The recommended daily dose is 100-150mg in two or three divided doses. For milder cases, 75-100mg daily in two or three divided doses is usually sufficient.

In migraine an initial dose of 50mg should be taken at the first signs of an impending attack. In cases where relief 2 hours after the first dose is not sufficient, a further dose of 50mg may be taken. If needed, further doses of 50mg may be taken at intervals of 4-6 hours, not exceeding a total dose of 200mg per day.

Special populations

**Paediatric population**

For children over 14 years of age, the recommended daily dose is 75-100mg in two or three divided doses. Diclofenac Potassium Caplets are not recommended for children under 14 years of age.

The use of Diclofenac Potassium caplets in migraine attacks has not been established in children.

**Elderly**

Although the pharmacokinetics of diclofenac 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 (see also precautions) and the patient should be monitored for GI bleeding during NSAID therapy.

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 (see section 4.3 Contraindications).

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.

**Method of administration**

For oral Route Administration

It is recommended that the caplets be taken with fluid, preferably with or after food.

**4.3 Contraindications**

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

• Active, gastric or intestinal ulcer, bleeding or perforation.

• History of gastrointestinal bleeding or perforation, relating to previous NSAID therapy.

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

• Last trimester of pregnancy (see section 4.6 Pregnancy and lactation).

• 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, angioedema, urticaria or acute rhinitis are precipitated by ibuprofen, acetylsalicylic acid or other nonsteroidal anti-inflammatory drugs.

• This product contains soya. If you are allergic to peanut or soya, do not use this medicinal product.

**4.4 Special warnings and precautions for use**

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

The concomitant use of diclofenac 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 (see section 4.5 Interactions with other medicaments and other forms of interaction).

Caution is indicated in the elderly on basic medical grounds. In particular, it is recommended that the lowest effective dose be used in frail elderly patients or those with a low body weight (see section 4.2 Posology and Method of administration).

As with other nonsteroidal anti-inflammatory drugs including diclofenac, allergic reactions, including anaphylactic/anaphylactoid reactions, can also occur without earlier exposure to the drug (see section 4.8 Undesirable effects). Hypersensitivity reactions can also progress to Kounis syndrome, a serious allergic reaction that can result in myocardial infarction. Presenting symptoms of such reactions can include chest pain occurring in association with an allergic reaction to diclofenac.

Like other NSAIDs, diclofenac may mask the signs and symptoms of the infection due to its pharmacodynamic properties.

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

The following interactions include those observed with diclofenac potassium caplets and/or other pharmaceutical forms of 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. beta-blockers, angiotensin converting enzyme (ACE) inhibitors may cause a decrease in their antihypertensive effect via inhibition of vasodilatory 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 periodically thereafter, particularly for diuretics and ACE inhibitors due to the increased risk of nephrotoxicity.

**4.6 Pregnancy and Lactation**

**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 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%.

The risk is believed to increase with dose and duration of therapy. In animals, administration of a prostaglandin synthesis inhibitor has 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 organogenetic period. If diclofenac is used by a woman attempting to conceive, or during the 1st trimesters 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 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, diclofenac is contra-indicated 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 (see section 5.2 Pharmacokinetic properties).

**Female 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 may 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 operating machinery.

**4.8 Undesirable effects**

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 doses (150mg daily) and in long term treatment.

### 4.9 Overdose

**a) Symptoms**

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

**b) Therapeutic measure**

Patients should be treated symptomatically as required.
Within one hour of ingestion of a potentially toxic amount, activated charcoal should be considered. Alternatively, in adults, gastric lavage should be considered within one hour of ingestion of a potentially life-threatening overdose.

## 5.0 PHARMACOLOGICAL PROPERTIES

### 5.1 Pharmacodynamics properties

EGMP Diclofenac Potassium caplets contain the potassium salt of diclofenac, a non-steroidal compound with pronounced and clinically demonstrable analgesic, anti-inflammatory and anti-pyretic properties.

EGMP Diclofenac is a potent inhibitor of prostaglandin biosynthesis and a modulator of arachidonic acid release and uptake.

EGMP Diclofenac Potassium caplets have a rapid onset of action and are therefore suitable for the treatment of acute episodes of pain and inflammation.

In migraine attacks EGMP Diclofenac Potassium caplets have been shown to be effective in relieving the headache and in improving the accompanying symptom of nausea.

Diclofenac in vitro does not suppress proteoglycan biosynthesis in cartilage at concentrations equivalent to the concentrations reached in human beings.

## 5.2 Pharmacokinetic properties

### Absorption

EGMP Diclofenac is rapidly and completely absorbed from sugar-coated caplets. Food intake does not affect absorption.

Peak plasma concentration after one 50 mg sugar-coated tablet was 3.9 µmol/l after 20-60 minutes. The plasma concentrations show a linear relationship to the size of the dose.

Diclofenac undergoes first-pass metabolism and is extensively metabolised.

### Distribution

Diclofenac is highly bound to plasma proteins (99.7%), chiefly albumin (99.4%)

Diclofenac was detected in a low concentration (100ng/mL) in breast milk in one nursing mother. The estimated amount ingested by infant consuming breast milk is equivalent to a 0.03 mg/kg/day dose (see section 4.6 Pregnancy and lactation).

### Route of Elimination

The total systemic clearance of diclofenac in plasma is 263 ± 56 ml/min (mean ± SD).
The terminal half-life in plasma is 1 – 2 hours.

Repeated oral administration of EGMP Diclofenac Potassium caplets for 8 days in daily doses of 50 mg t.d.s does not lead to accumulation of diclofenac in the plasma.

Approx. 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.

## 5.3 Preclinical safety data

There are no pre-clinical data of relevance to the prescriber

## 6.0 PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients

| S/NO | INGREDIENTS | QUANTITY/5ml (KG) |
|---|---|---|
| 1 | Corn starch | 76kg |
| 2 | Povidone | 2.0kg |
| 3 | Sodium methyl paraben | 0.12kg |
| 4 | Sodium propyl paraben | 0.04kg |
| 5 | Talc powder | 0.9kg |
| 6 | Magnesium stearate | 0.6kg |

### 6.2 Incompatibilities

Not applicable.

### 6.3 Shelflife

36 months

### 6.4 Storage

Keep tightly closed, in a cool dry place at or below 30°C away from sunlight.

Store in original package.

### 6.5 Nature and contents of container

Blisters of 10x10 caplets with EGMP written on the foil on one side and plain PVC on the other.

### 6.6Special precautions for disposal and handling:

No special requirements.

## 7.0 APPLICANT/MANUFACTURER

### 7.1 Name and Address

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